NCBI

MIM *109091

Gene map

LocusLink

LinkOut

SYSTEM:OS - DIALOG OneSearch
File 5:Biosis Previews(R) 1969-2003/Jan W3
(c) 2003 BIOSIS
***File 5: Alert feature enhanced for multiple files, duplicates** removal, customized scheduling. See HELP ALERT.
File 34:SciSearch(R) Cited Ref Sci 1990-2003/Jan W3
(c) 2003 Inst for Sci Info
***File 34: Alert feature enhanced for multiple files, duplicates** removal, customized scheduling. See HELP ALERT.
File 155:MEDLINE(R) 1966-2003/Jan W3
***File 155: Updating of completed records has resumed.See Help News155.**
Alert feature enhanced with customized scheduling. See HELP ALERT.

Set	Items	Description
S1	100	VASO AND BONE(W)MARROW
S2	0	S1 AND CALRETICULIN
S3	1	S1 AND RO?
S4	112	VASOSTATIN
S5	1	S4 AND BONE(W)MARROW

8/9/4 (Item 4 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

13446559 BIOSIS NO.: 200200075380
The angiogenesis inhibitor vasostatin **does not impair wound healing at tumor-inhibiting doses.**
AUTHOR: Lange-Asschenfeldt Bernhard; Velasco Paula; Streit Michael; Hawighorst Thomas; Pike Sandra E; Tosato Giovanna; Detmar Michael(a)
AUTHOR ADDRESS: (a)Cutaneous Biology Research Center, Department of Dermatology, Massachusetts General Hospital, 13th Street, Building 149, Charlestown, MA, 02129**USA E-Mail: michael.detmar@cbrc2.mgh.harvard.edu
JOURNAL: Journal of Investigative Dermatology 117 (5):p1036-1041 November, 2001
MEDIUM: print
ISSN: 0022-202X
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Inhibition of tumor angiogenesis represents a promising new approach for the treatment of human cancers. It has remained unclear, however, whether inhibition of tumor angiogenesis may also result in impaired wound healing, a process thought to be angiogenesis dependent. To determine the effects of the angiogenesis inhibitor **vasostatin** , a 180 amino acid calreticulin fragment, on wound healing at tumor inhibiting doses, full-thickness wounds were generated on the back of nude mice that were also injected intradermally with CA46 Burkitt lymphoma cells. Mice were treated with daily injections of **vasostatin** or vehicle control at a site between the wounds and the transplanted tumor cells over 14 d. **Vasostatin** potently inhibited tumor growth and significantly reduced tumor angiogenesis, as measured by computer-assisted image analysis of CD31-stained tumor sections. Moreover, **vasostatin** treatment resulted in an increased fraction of mature tumor-associated **blood** vessels. In contrast, no impairment of wound healing was observed in **vasostatin** -treated mice, despite a significantly reduced vascularity of the wound granulation tissue. Our results reveal a different sensitivity of malignant tumor growth and physiologic wound healing to inhibition of angiogenesis, and they suggest that therapeutic inhibition of tumor angiogenesis may be achieved without impairment of tissue repair.

8/9/19 (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08529247 95285641 PMID: 7768066
Chromogranin A.
Hendy G N; Bevan S; Mattei M G; Mouland A J
Calcium Research Laboratory, McGill University, Montreal, Quebec.
Clinical and investigative medicine. Medecine clinique et experimentale (CANADA) Feb 1995, 18 (1) p47-65, ISSN 0147-958X Journal Code:

7804071
Document type: Journal Article; Review; Review, Tutorial
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS

Chromogranin A (CgA) is the major member of the granin family of acidic secretory glycoproteins that are expressed in all endocrine and neuroendocrine cells. Granins have been proposed to play multiple roles in the secretory process. Intracellularly, granins play a role in targeting peptide hormones and neurotransmitters to granules of the regulated pathway by virtue of their ability to aggregate in the low-pH, high-calcium environment of the trans-Golgi network. Extra-cellularly, peptides formed as a result of proteolytic processing of granins regulate hormone secretion. Some conserved features of the mature CgA protein are polyglutamic acids, calcium-binding sites, and several pairs of basic amino acids. The first 2 features are important for its intracellular functions, and the latter characteristic suggested that peptides could be released from the molecule by precursor processing enzymes. Several biologically active peptides encoded within the CgA molecule, such as **vasostatin** , beta-granin, chromostatin, pancreastatin, and parastatin act predominantly to inhibit hormone and neurotransmitter release in an autocrine or paracrine fashion. The biosynthesis of CgA is regulated by many different factors, including steroid hormones and agents that act through a variety of signalling pathways. CgA biosynthesis and that of the resident hormone or neurotransmitter can be regulated differentially. The widespread distribution of CgA has made the measurement of circulating immunoreactive CgA a valuable tool in the diagnosis of neuroendocrine neoplasia, and CgA immunohistochemistry can help to identify the neuroendocrine nature of tumours. Recent molecular biology studies are identifying those elements in the CgA gene promoter responsible for its specific neuroendocrine cell expression. (116 Refs.)

Set	Items	Description
S1	100	VASO AND BONE(W)MARROW
S2	0	S1 AND CALRETICULIN
S3	1	S1 AND RO?
S4	112	VASOSTATIN
S5	1	S4 AND BONE(W)MARROW
S6	25475	DS
S7	31	S4 AND (BLOOD OR HEMATOP?)
S8	19	RD (unique items)

WEST

The Contents of Case 09828000

Qnum	Query	DB Name	Thesaurus	Operator	Plural
Q1	vasostatin	USPT	ASSIGNEE	ADJ	YES
Q2	calreticulin	USPT	ASSIGNEE	ADJ	YES
Q3	Q2 and hematopoi$3	USPT	ASSIGNEE	ADJ	YES
Q4	Q2 and bone marrow	USPT	ASSIGNEE	ADJ	YES

Run Case | Update Case | Cancel

Help | Main Menu | Logout

***109091**

Links

CALRETICULIN; CALR

Alternative titles; symbols

AUTOANTIGEN Ro; RO

Gene map locus 19p13.2

TEXT

Calreticulin is a multifunctional protein that acts as a major Ca(2+)-binding (storage) protein in the lumen of the endoplasmic reticulum. It is also found in the nucleus, suggesting that it may have a role in transcription regulation. Calreticulin binds to the synthetic peptide KLGFFKR, which is almost identical to an amino acid sequence in the DNA-binding domain of the superfamily of nuclear receptors. McCauliffe et al. (1990) showed that calreticulin binds to antibodies in certain sera of systemic lupus and Sjogren patients which contain anti-Ro/SSA antibodies, that it is highly conserved among species, and that it is located in the endoplasmic and sarcoplasmic reticulum where it may bind calcium. With synthetic oligonucleotides corresponding to the amino acid sequence, McCauliffe et al. (1990) isolated a full-length cDNA clone that encodes a human Ro ribonucleoprotein autoantigen. Southern filter hybridization analysis showed that the gene is not highly polymorphic and exists in single copy in the human genome. By analysis of somatic cell hybrids, they assigned the gene to 19p. There was perfect concordance with LDLR (606945) but discordance with C3 (120700). Thus, the calreticulin, or RO, locus may be located in the region 19pter-p13.2, distal to C3 and near LDLR. Frank (1994) pointed out that the gene mapped to 19p encodes the 48-kD calreticulin, a protein with Ro/SSA properties. Itoh et al. (1991) showed that the 52-kD and the 60-kD forms of Ro/SSA ribonucleoproteins are encoded by separate genes. The gene for the 52-kD form (109092) maps to chromosome 11, whereas the gene for the 60-kD form (600063) maps to chromosome 1.

Burns et al. (1994) reported that the amino terminus of calreticulin interacts with the DNA-binding domain of the glucocorticoid receptor and prevents the receptor from binding to its specific glucocorticoid response element. Dedhar et al. (1994) showed that calreticulin can inhibit the binding of androgen receptor to its hormone-responsive DNA element and can inhibit androgen receptor and retinoic acid receptor transcriptional activities in vivo, as well as retinoic acid-induced neuronal

differentiation. Thus, calreticulin can act as an important modulator of the regulation of gene transcription by nuclear hormone receptors.

Boehm et al. (1994) showed that SLE is associated with increased autoantibody titers against calreticulin but that calreticulin is not a Ro/SS-A antigen. Orth et al. (1996) found increased autoantibody titers against human calreticulin in infants with complete congenital heart block (234700) of both the IgG and IgM classes.

Rooke et al. (1997) mapped the homologous mouse gene, Calr, to mouse chromosome 8.

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PubMed ID : 8107808

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PubMed ID : 8107809

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Personal Communication. Oklahoma City, Okla., 6/3/1994.

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PubMed ID : 1985094

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Molecular cloning, expression, and chromosome 19 localization of a human Ro/SS-A autoantigen. *J. Clin. Invest.* 85: 1379-1391, 1990.
PubMed ID : 2332496

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A human Ro/SS-A autoantigen is the homologue of calreticulin and is highly homologous with onchocercal RAL-1 antigen and an aplysia 'memory molecule.'. *J. Clin. Invest.* 86: 332-335, 1990.
PubMed ID : 2365822

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Complete congenital heart block is associated with increased autoantibody titers against calreticulin. *Europ. J. Clin. Invest.* 26: 205-215, 1996.
PubMed ID : 8904349

9. Rooke, K.; Briquet-Laugier, V.; Xia, Y.-R.; Lusis, A. J.; Doolittle, M. H. :
Mapping of the gene for calreticulin (Calr) to mouse chromosome 8. *Mammalian Genome* 8: 870-871, 1997.
PubMed ID : 9337407

CONTRIBUTORS

Victor A. McKusick - updated : 11/21/1997

CREATION DATE

Victor A. McKusick : 8/15/1990

EDIT HISTORY

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terry : 11/26/1997
terry : 11/21/1997
terry : 5/2/1996
mark : 4/27/1996
terry : 4/22/1996
carol : 11/30/1994
jason : 7/28/1994
mimadm : 4/21/1994
pfoster : 3/25/1994
carol : 3/1/1993
carol : 5/22/1992

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):0

=> fil hcaplu
FILE 'HCAPLUS' ENTERED AT 15:51:31 ON 01 FEB 2002

FILE COVERS 1907 - 1 Feb 2002 VOL 136 ISS 6
FILE LAST UPDATED: 30 Jan 2002 (20020130/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

CAS roles have been modified effective December 16, 2001. Please check your SDI profiles to see if they need to be revised. For information on CAS roles, enter HELP ROLES at an arrow prompt or use the CAS Roles thesaurus (/RL field) in this file.

The P indicator for Preparations was not generated for all of the CAS Registry Numbers that were added to the CAS files between 12/27/01 and 1/23/02. As of 1/23/02, the situation has been resolved. Searches and/or SDIs in the H/Z/CA/CAplus files incorporating CAS Registry Numbers with the P indicator executed between 12/27/01 and 1/23/02 may be incomplete. See the NEWS message on this topic for more information.

=> d stat que
L1 18887 SEA FILE=HCAPLUS "RADIATION DAMAGE"/CV OR (RADIOPROTECTANTS/CV OR RADIOTHERAPY/CV) OR "RADIATION SICKNESS"/CV
L2 63637 SEA FILE=HCAPLUS BONE(W)MARROW OR (HEMATOPOIE? OR LIN OR CD34?)(2A)CELL?
L3 1161 SEA FILE=HCAPLUS L1 AND L2
L4 (3)SEA FILE=REGISTRY FUSION PEPTIDE?/CN
L5 (129)SEA FILE=REGISTRY FUSION PROTEIN?/CN
L6 (2)SEA FILE=REGISTRY MALTOSE/CN
L7 (2338)SEA FILE=REGISTRY HHHHHH/SQSP
L8 (756)SEA FILE=HCAPLUS L4 OR FUSION(W)PEPTIDE?
L9 (27614)SEA FILE=HCAPLUS L8 OR L5 OR FUSION(W)PROTEIN?
L10 (23439)SEA FILE=HCAPLUS L6 OR MALTOSE?
L11 (1379)SEA FILE=HCAPLUS HIS(2W)HIS(2W)HIS(2W)HIS(2W)HIS OR L7
L12 112337 SEA FILE=HCAPLUS L9 OR L10 OR L11 OR GLUTATHIONE? OR CARRIER(W)PEPTIDE
L13 43 SEA FILE=HCAPLUS L3 AND L12

=> d ibib abs hitrn l13 1-43

L13 ANSWER 1 OF 43 HCAPLUS COPYRIGHT 2002 ACS.
ACCESSION NUMBER: 2001:916371 HCAPLUS
DOCUMENT NUMBER: 136:52722
TITLE: Protein tyrosine kinase agonist antibodies
INVENTOR(S): Bennett, Brian D.; Goeddel, David; Lee, James M.; Matthews, William; Tsai, Siao Ping; Wood, William I.
PATENT ASSIGNEE(S): Genentech, Inc., USA
SOURCE: U.S., 113 pp., Cont.-in-part of U.S. 5,635,177.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6331302	B1	20011218	US 1996-446648	19960523
WO 9315201	A1	19930805	WO 1993-US586	19930122
W: AU, CA, JP, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 5635177	A	19970603	US 1994-222616	19940404
WO 9527061	A1	19951012	WO 1995-US4228	19950404
W: CA, JP, MX, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				

PRIORITY APPLN. INFO.:
US 1992-826935 B2 19920122
WO 1993-US586 A2 19930122
US 1994-222616 A2 19940404
US 1994-256769 A 19940915
WO 1995-US4228 W 19950404

AB Agonist antibodies are disclosed which bind to the extracellular domain of receptor protein tyrosine kinases pTKs, and thereby cause dimerization and activation of the intracellular tyrosine kinase domain thereof. The antibodies are useful for activating their resp. receptor and thereby enabling the role of the tyrosine kinase receptor in cell growth and/or differentiation to be studied. Chimeric proteins comprising the extracellular domain of the receptor pTKs and an Ig const. domain sequence are also disclosed.

REFERENCE COUNT: 65 THERE ARE 65 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 2 OF 43 HCAPLUS COPYRIGHT 2002 ACS.
ACCESSION NUMBER: 2001:833064 HCAPLUS
DOCUMENT NUMBER: 135:352781
TITLE: Compositions and methods for protecting cells during cancer chemotherapy and radiotherapy
INVENTOR(S): Fahl, William E.; Raghavachari, Nalimi; Zhu, Ming; Kink, John
PATENT ASSIGNEE(S): Wisconsin Alumni Research Foundation, USA
SOURCE: PCT Int. Appl., 75 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001085142	A1	20011115	WO 2001-US14464	20010504

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2000-565714 A 20000505

AB Compns., pharmaceutical prepns. and methods are disclosed for protecting non-neoplastic cells from damage caused by cancer chemotherapeutic agents or radiation therapy, during the course of cancer therapy or **bone marrow** transplant. These are based on the use of chemoprotective inducing agents that induce or increase prodn. of cellular detoxification enzymes in target cell populations. The compns. and methods are useful to reduce or prevent hair loss, gastrointestinal distress and lesions of the skin and oral mucosa that commonly occur in patients undergoing cancer therapy. Also disclosed is a novel assay system for identifying new chemoprotective inducing agents.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 3 OF 43 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:798032 HCAPLUS
DOCUMENT NUMBER: 135:327377
TITLE: Administration of a thiol-based chemoprotectant compound
INVENTOR(S): Pagel, Michael A.; Muldoon, Leslie; Neuwelt, Edward A.
PATENT ASSIGNEE(S): Oregon Health Sciences University, USA; Government of the United States; Department of Veterans Affairs
SOURCE: PCT Int. Appl., 46 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001080832	A2	20011101	WO 2001-US40624	20010426

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ,

VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
PRIORITY APPLN. INFO.: US 2000-199936 P 20000426
US 2000-229870 P 20000830

AB A method of administration of a thiol-based chemoprotectant agent including NAC (N-acetylcysteine) and STS (sodium thiosulfate) that markedly affects biodistribution and protects against injury from diagnostic or therapeutic intra-arterial procedures. A method for treating or mitigating the side effects of cytotoxic cancer therapy for tumors located in the head or neck and brain tumors. The thiol-based chemoprotectant agent is administered intra-arterially with rapid and first pass uptake in organs and tissues other than the liver.

L13 ANSWER 4 OF 43 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:731002 HCAPLUS
DOCUMENT NUMBER: 135:283176
TITLE: Anti-angiogenic and anti-tumor properties of Matin (globular G1 domain of .alpha.1 chain of laminin) and other laminin domains
INVENTOR(S): Kalluri, Raghuram
PATENT ASSIGNEE(S): Beth Israel Deaconess Medical Center, USA
SOURCE: PCT Int. Appl., 78 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001073033	A2	20011004	WO 2001-US9921	20010328

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
PRIORITY APPLN. INFO.: US 2000-192875 P 20000329

AB A protein, designated "Matin", comprising the globular G1 domain of .alpha.1 chain of laminin with anti-angiogenic and anti-tumor properties is disclosed. Laminin is the most abundant noncollagenous protein found in basement membranes. Matin is a monomeric protein, about 30 kDa, and arrests endothelial cell proliferation in vivo. The Matin can be the G1 domain of the .alpha.1 chain of another laminin, other globular domains, laminin from other mammals, and fragments, mutants, homologs, analogs and allelic variants of the Matin amino acid sequence. The invention relates to Matin-contg. chimeric protein which can further comprise Vascostatin, Arresten, Canstatin, Tumstatin, endostatin, angiostatin, Restin, Apomigren, or other anti-angiogenic proteins or fragments thereof.

L13 ANSWER 5 OF 43 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:730994 HCAPLUS
DOCUMENT NUMBER: 135:267222
TITLE: Anti-angiogenic and anti-tumor properties of Vascostatin (C-terminal globular domain of nidogen/entactin-1) and other nidogen domains
INVENTOR(S): Kalluri, Raghuram
PATENT ASSIGNEE(S): Beth Israel Deaconess Medical Center, USA
SOURCE: PCT Int. Appl., 66 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001073025	A2	20011004	WO 2001-US40382	20010328

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2000-192871 P 20000329
AB A protein, designated "Vascostatin", comprising the C-terminal globular domain of nidogen-1 with anti-angiogenic and anti-tumor properties is disclosed. Nidogen, also known as entactin, is a component of basement membranes, and is often found with lamanin. Vascostatin is a monomeric protein, about 20 kDa, and arrests endothelial cell proliferation in vivo. The Vascostatin can be the C-terminal globular domain of another nidogen, nidogen from other mammals, and fragments, mutants, homologs, analogs and allelic variants of the Vascostatin amino acid sequence. The invention relates to Vascostatin-contg. chimeric protein which can further comprise Matin, Arresten, Canstatin, Tumstatin, endostatin, angiostatin, Restin, Apomigren, or other anti-angiogenic proteins or fragments thereof.

L13 ANSWER 6 OF 43 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:507851 HCAPLUS
DOCUMENT NUMBER: 135:117945
TITLE: Cloning and use of the FRIL family of progenitor cell preservation factors
INVENTOR(S): Colucci, M. Gabriella; Chrispeels, Maarten J.; Moore, Jeffrey G.
PATENT ASSIGNEE(S): Phylogix LLC, USA
SOURCE: PCT Int. Appl., 172 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001049851	A1	20010712	WO 1999-US31307	19991230

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

AB Disclosed is the nucleic acids encoding three members of FRIL family, which are mannose-binding lectins, of progenitor cell preservation factors, including D1FRIL, Pv-FRIL and YamFRIL. FRIL family members preserve progenitor cells both in vivo and ex vivo. FRIL family members find use as therapeutics for alleviating and/or reducing the **hematopoietic** progenitor **cell**-depleting activity of many cancer therapeutics. Recombinant D1-FRIL specifically stimulates proliferation of 3T3 cells expressing the FLT3 receptor and preserves mononuclear cells and progenitors expressing CD34. D1-FRIL maintains the expansion capacity of CD34+ progenitors up to two weeks and SCID repopulating stem cells (SRC) in ex vivo culture, and maintains high levels of **CD34+ cells** in G0/G1 phase of cell cycle. D1-FRIL preserves SRC potential of multilineage differentiation and protects CB MNC from the toxicity of chemotherapy drugs. D1-FRIL-coated beads can be used to isolate progenitor **cells, CD34** -primitive stem **cells** and normal stem cells, dendritic progenitors and mature cells, endothelial stem cells and progenitors.

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 7 OF 43 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:417175 HCAPLUS
DOCUMENT NUMBER: 135:1218
TITLE: Dexamethasone inducible viral vector responding to host cell transcriptional activators and its therapeutic uses
INVENTOR(S): Galipeau, Jacques; Jaalouk, Diana E.; Eliopoulos, Nicoletta; Couture, Clement; Mader, Sylvie
PATENT ASSIGNEE(S): Centre for Translational Research In Cancer, Can.
SOURCE: PCT Int. Appl., 51 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001040494	A1	20010607	WO 2000-CA1422	20001130

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,

CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR,
HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT,
LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,
SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN,
YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 1999-168299 P 19991201

AB The present invention relates to a drug inducible vector regulatable with a trans-activator native to a host, and to a transplantable autologous tissue capable of engrafting in a recipient without requiring toxic conditioning, for transgene delivery to a recipient. Current drug inducible host-vector systems are responsive to foreign non-eukaryotic transcriptional activators which are potentially immunogenic and affect the long-term survival and function thereof. The present invention provides a drug inducible expression vector comprising a transgene operably linked to a reporter and to an inducible promoter responsive to a transcriptional activator of a host when exposed to an effective amt. of a clin. acceptable drug. Such a vector may be introduced in a transplantable host derived from the recipient and capable of engrafting in the recipient without requiring toxic conditioning. A retroviral vector using the GRE5 glucocorticoid-response element in the long terminal repeat to confer dexamethasone inducibility is described. Use of the vector to deliver a gene for erythropoietin under the very tight control of dexamethasone to rat **bone marrow** stroma is described.

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 8 OF 43 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:247459 HCAPLUS
DOCUMENT NUMBER: 134:294083
TITLE: Characterization and diagnostic and therapeutic uses of cancer-associated membrane type serine protease 1 (MT-SP1)
INVENTOR(S): Craik, Charles S.; Takeuchi, Toshihiko; Shuman, Marc
PATENT ASSIGNEE(S): The Regents of the University of California, USA
SOURCE: PCT Int. Appl., 102 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001023524	A2	20010405	WO 2000-US27250	20001002

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR,
HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT,
LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,
SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU,
ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

AU 2000079913 A5 20010430 AU 2000-79913 20001002

PRIORITY APPLN. INFO.: US 1999-410362 A 19990930
WO 2000-US27250 W 20001002

AB This invention provides cDNA and encoded amino acid sequences of a novel membrane-type serine protease (designated MT-SP1) elevated expression of which is assocd. with cancer. In one embodiment, this invention provides a method obtaining a prognosis or of detecting of staging a cancer in an organism. The method involves providing a biol. sample from the organism and detecting the level of a membrane-type serine protease 1 (MT-SP1) in the sample, where an elevated level of the membrane-type serine protease, as compared to the level of the protease in a biol. sample from a normal healthy organism indicates the presence or stage of the cancer.

L13 ANSWER 9 OF 43 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:179055 HCAPLUS

DOCUMENT NUMBER: 135:192250

TITLE: Modulation of radiation-induced organs toxicity by cremophor-el in experimental animals

AUTHOR(S): Ramadan, Laila A.; Shouman, Samia A.; Sayed-Ahmed, Mohamed M.; El-Habit, Ola H.

CORPORATE SOURCE: National Center for Radiation Research and Technology, Drug Radiation Research Department, Atomic Energy Authority, (NCRRT), Cairo, Egypt

SOURCE: Pharmacol. Res. (2001), 43(2), 185-191
CODEN: PHMREP; ISSN: 1043-6618

PUBLISHER: Academic Press

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Pharmacol. and cytogenetic evaluations of the protective effects of polyethoxylated castor oil cremophor-EL (cremophor) against hepato, renal and **bone marrow** toxicity induced by gamma irradn. in normal rats were carried out. A single dose of irradn. (6 Gy) caused hepatic and renal damage manifested biochem. as an elevation in levels of serum alanine and aspartate aminotransferase as well as an increase in blood urea. Cremophor administration at a dose level of 50 .mu.l kg-1 i.v. 1 day before exposure to irradn. (6 Gy) protected the liver and kidney as indicated by the recovery of levels of hepatic aminotransferase, urea and lipid profiles to normal values. Gamma irradn. of male rats caused a decrease in reduced **glutathione** and an increase in the oxidized form in rat-liver homogenate. A highly significant increase in the incidence of micronucleated normochromatic erythrocytes and micronucleated polychromatic erythrocytes was obsd. after irradn. exposure. The induced genotoxicity in the **bone marrow** cells was cor. by pretreatment with cremophor. The findings of this study suggest that cremophor pretreatment can potentially be used clin. to prevent irradn.-induced hepato, renal and **bone marrow** toxicity without interference with its cytotoxic activity. (c) 2001 The Italian Pharmacological Society.

REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 10 OF 43 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:115001 HCAPLUS
DOCUMENT NUMBER: 134:177355
TITLE: Treatment of intermediate- and high-grade non-Hodgkins lymphoma with anti-CD20 antibody
INVENTOR(S): White, Christine A.; Grillo-Lopez, Antonio
PATENT ASSIGNEE(S): Idec Pharmaceuticals Corporation, USA
SOURCE: PCT Int. Appl., 21 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001010460	A1	20010215	WO 2000-US19563	20000802

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 1999-148286 P 19990811
US 2000-628187 A 20000728

AB This invention discloses methods for the treatment of intermediate- and high-grade non-Hodgkins lymphomas comprising administration of anti-CD20 antibodies.

REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 11 OF 43 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:456902 HCAPLUS
DOCUMENT NUMBER: 133:84274
TITLE: Protection of **hematopoietic cells** by the induction of post-mitotic quiescence
INVENTOR(S): Korkut, Edib
PATENT ASSIGNEE(S): USA
SOURCE: PCT Int. Appl., 18 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000038705	A1	20000706	WO 1999-US29575	19991215

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA,

MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

US 2001039259 A1 20011108 US 2001-881669 20010618
PRIORITY APPLN. INFO.: US 1998-220677 A 19981223
US 1998-96533 P 19980813

AB Methods are provided for minimizing the toxic effects of chemotherapy or cytotoxic irradn. on the **hematopoietic cells** of a patient having neoplastic cells or a malignant tumor. The methods comprise treating the patient with a dosage of at least one **hematopoietic cell** stimulating factor, the dosage being sufficient in amt. and time to cause a substantial increase in the population of the **hematopoietic cells** and in differentiated blood cells, and then treating the patient with a dosage of chemotherapeutic agents or cytotoxic irradn. sufficient to substantially reduce the population of neoplastic or cancerous cells. The methods increase the abs. no. of **hematopoietic** progenitor **cells** and differentiated cells in the patient's blood system prior to the administration of therapeutic insult thereby increasing the no. of **hematopoietic** progenitor **cells** and differentiated cells which survive therapeutic insult.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 12 OF 43 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:410180 HCAPLUS
DOCUMENT NUMBER: 133:131827
TITLE: Radioprotective effects of the thiols GSH and WR-2721 against X-ray-induction of micronuclei in erythroblasts
AUTHOR(S): Mazur, L.
CORPORATE SOURCE: R. Ingardena 6, Institute of Zoology, Department of Animal Physiology, Laboratory of Experimental Haematology and Toxicology, Jagiellonian University, Krakow, 30-060, Pol.
SOURCE: Mutat. Res. (2000), 468(1), 27-33
CODEN: MUREAV; ISSN: 0027-5107
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The frequency of micronucleated polychromatic erythrocytes (MNPCEs) was assessed in the **bone marrow** and peripheral blood of adult male Swiss mice treated with reduced **glutathione** (GSH) and S-2-/3-aminopropylamino/ethyl phosphorothioic acid (WR-2721), at a dose of 400 mg/kg body wt., and exposed to 6 Gy X-rays. GSH or WR-2721 was applied alone, or 60 and 30 min, resp., prior to X-ray-exposure. The no. of MNPCEs was detd. at 24 h after the thiol treatment and X-irradn. The radioprotection and toxicity caused in the mouse erythroblasts by GSH and WR-2721, as indicated by the no. of MNPCEs were dependent on the thiol applied. The stronger radioprotective effect is obtained following WR-2721 administration than after GSH application. WR-2721 showed greater

toxicity than GSH. The combination of GSH and WR-2721 given before X-ray-exposure resulted in the most radioprotective effect as compared to the resp. single-drug treatment of mice. Application of the both thiols, without subsequent X-irradn. appeared to be the most toxic, compared with administration of WR-2721 or GSH alone. The effective radioprotection by the combined action of GSH and WR-2721 against genomic instability induced in the mouse erythroblasts by X-rays was shown.

REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 13 OF 43 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:133559 HCAPLUS
DOCUMENT NUMBER: 132:179588
TITLE: Combination therapies for B-cell lymphomas comprising administration of anti-CD20 antibody
INVENTOR(S): Grillo-Lopez, Antonio
PATENT ASSIGNEE(S): Idec Pharmaceuticals Corporation, USA
SOURCE: PCT Int. Appl., 52 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000009160	A1	20000224	WO 1999-US18120	19990811
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9955531	A1	20000306	AU 1999-55531	19990811
EP 1112084	A1	20010704	EP 1999-942074	19990811
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
BR 9913645	A	20010925	BR 1999-13645	19990811
NO 2001000699	A	20010410	NO 2001-699	20010209

PRIORITY APPLN. INFO.: US 1998-96180 P 19980811
WO 1999-US18120 W 19990811

AB New combined therapeutic regimens for treatment of B-cell lymphomas are disclosed which comprise in particular administration of anti-CD20 antibodies to patients having low-, intermediate- or high-grade non-Hodgkins lymphomas. The anti-CD20 antibody may be administered in combination with cytokines, radiotherapy, myeloblastive (i.e. **bone marrow** or stem cell transplant) therapy, or chemotherapy.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 14 OF 43 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2000:84818 HCAPLUS
DOCUMENT NUMBER: 132:118360
TITLE: Angiopoietin-related gene Scarface 2 and its human protein product
INVENTOR(S): Burgett, Stanley Gene; Leonard, Rebecca Ann; Rosteck, Paul Robert, Jr.; Sankhavaram, Patanjali
PATENT ASSIGNEE(S): Eli Lilly and Company, USA
SOURCE: PCT Int. Appl., 85 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000005241	A1	20000203	WO 1999-US15675	19990712
W: AE, AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9952108	A1	20000214	AU 1999-52108	19990712
EP 995759	A1	20000426	EP 1999-305510	19990712
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				

PRIORITY APPLN. INFO.: US 1998-94033 P 19980724
WO 1999-US15675 W 19990712

AB The invention provides isolated human Scarface 2 nucleic acid compds., proteins and fragments thereof. Scarface is a member of a family of related Scarface proteins, including mammalian angiopoietin 1 and angiopoietin 2 and to Drosophila Scabrous protein, and contains a fibrinogen-like domain and a coiled-coil domain. Scarface 2 is expressed in multiple tissues and cell types including kidney tubule cells and liver. Also provided are vectors and transformed heterologous host cells for expressing Scarface 2, methods for identifying compds. that bind and/or modulate the activity of said Scarface 2 proteins, as well as methods for treating cancer, and pharmaceutical compns. The invention also provides a method for treating soft tissue cancers including leukemias, and methods for suppressing the growth of stem **cells** including **hematopoietic** progenitor **cells**, and/or to prevent the expansion of said cells during chemotherapy or radiotherapy.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 15 OF 43 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:78481 HCAPLUS
DOCUMENT NUMBER: 133:57351
TITLE: Therapeutic effect of **fusion protein** G3 containing interleukin 3 and GM-CSF in rhesus monkeys with **bone marrow** type acute radiation sickness

AUTHOR(S): Chen, Guanying; Gong, Manli; Lu, Jia; Zhao, Huiyun; Shen, Qinjian; Zhou, Mei
CORPORATE SOURCE: Department of Radiation Medicine, Beijing Medical University, Beijing, 100083, Peop. Rep. China
SOURCE: Zhonghua Fangshe Yixue Yu Fanghu Zazhi (1999), 19(6), 375-378
CODEN: ZFYZDY; ISSN: 0254-5098
PUBLISHER: Weishengbu Gongye Weisheng Shiyanso
DOCUMENT TYPE: Journal
LANGUAGE: Chinese

AB Twenty normal rhesus monkeys were subjected to 4.0 Gy total-body irradn. (TBI) and randomly divided into 4 groups (5 each) to explore the effect of **fusion protein** G3 contg. interleukin 3 and GM-CSF (rhGM-CSF/rhIL3 F.P) on increasing the nos. of leukocytes and platelets in rhesus monkeys with **bone marrow** type acute radiation sickness. Protein G3 of 40 or 20 .mu.g/kg.d was s.c. injected for 20 days in the exptl. group, whereas Leucomax (GM-CSF) at 20 .mu.g/kg.d was s.c. injected for 20 days in the control group. The recovering peak values of WBC, ANC and PLT in the groups with G3 were higher than the controls. Protein G3 was effective in reducing the periods of low-level WBC, ANC and PLT. Protein G3 was therapeutic for the radiation sickness in myelosuppressed rhesus monkeys.

L13 ANSWER 16 OF 43 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:682734 HCAPLUS
DOCUMENT NUMBER: 132:233683
TITLE: Influence of rhTPO/GM-CSF **fusion protein** on hemopoiesis in mice irradiated with 60Co .gamma.-rays
AUTHOR(S): Cao, Hua; Ge, Zhongliang; Zhang, Qunwei; Liu, Xiuzhen
CORPORATE SOURCE: Institute of Radiation Medicine, Beijing, 100850, Peop. Rep. China
SOURCE: Zhonghua Fangshe Yixue Yu Fanghu Zazhi (1999), 19(4), 251-253
CODEN: ZFYZDY; ISSN: 0254-5098
PUBLISHER: Weishengbu Gongye Weisheng Shiyanso
DOCUMENT TYPE: Journal
LANGUAGE: Chinese

AB HGMCSF gene was ligated with hTPO gene isolated from human fetal liver mRNA and a new **fusion protein** rhTPO/GM-CSF obtained to find a new biol. therapy for secondary hematopoietic failure including anemia, infection and hemorrhage after administration of chemotherapeutic drugs etc. The new **fusion protein** could promote recovery of peripheral WBC and PLT of 5.0 Gy irradiated mice. BFU-E, CFU-Meg and CFU-GM in **bone marrow** of mice after irradn. recovered significantly by treatment with rhTPO/GM-CSF **fusion protein** for 10 days. These results suggest that the new **fusion protein** has the biol. activity of both hTPO and hGM-CSF simultaneously and can stimulate the proliferation of megakaryocyte and granulocyte progenitors.

L13 ANSWER 17 OF 43 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:644154 HCAPLUS
DOCUMENT NUMBER: 131:335722

TITLE: Stable mixed hematopoietic chimerism in dogs given donor antigen, CTLA4Ig, and 100 cGy total body irradiation before and pharmacologic immunosuppression after marrow transplant

AUTHOR(S): Storb, Rainer; Yu, Cong; Zaucha, J. Maciej; Deeg, H. Joachim; Georges, George; Kiem, Hans-Peter; Nash, Richard A.; McSweeney, Peter A.; Wagner, John L.

CORPORATE SOURCE: Clinical Research Division, Fred Hutchinson Cancer Research Center, Seattle, WA, 98109-1024, USA

SOURCE: Blood (1999), 94(7), 2523-2529
CODEN: BLOOAW; ISSN: 0006-4971

PUBLISHER: W. B. Saunders Co.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Stable mixed chimerism can be established in dogs given a sublethal dose of 200 cGy total body irradn. (TBI) before and immunosuppression with mycophenolate mofetil (MMF) and cyclosporine (CSP) for 28 and 35 days, resp., after dog leukocyte antigen-identical marrow transplantation. Most likely, the role of pretransplant TBI was to provide host immunosuppression, since stable mixed chimerism was also achieved in MMF/CSP-treated dogs when 450 cGy irradn., targeted to cervical, thoracic, and upper abdominal lymph nodes, was substituted for TBI. When TBI was reduced from 200 to 100 cGy, all grafts were rejected within 3 to 12 wk. Here, we asked whether stable engraftment after 100 cGy TBI could be accomplished by first reducing the intensity of host immune responsiveness with help of the **fusion peptide** CTLA4Ig, which blocks T-cell costimulation through the B7-CD28 signal pathway. Accordingly, recipient T cells were activated with i.v. injections of 106 donor peripheral blood mononuclear cells (PBMC)/kg per day on days -7 to -1 before 100 cGy TBI, with concurrent administration of CTLA4Ig 4 mg/kg/d IV. All 7 dogs so treated showed initial mixed chimerism. Two rejected their allografts after 8 and 20 wk, resp., and survived with autologous marrow recovery; 1 mixed chimera was unevaluable because of death at 3 wk from intussusception; and 4 showed persisting mixed chimerism, including unirradiated marrow and lymph node spaces, for now more than 46 to 70 wk after transplant. Data support the hypothesis that stable marrow allografts can be established by combining nonmyeloablative pretransplant host immunosuppression with posttransplant host and donor cell immunosuppression using MMF/CSP.

REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 18 OF 43 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1999:606964 HCAPLUS

DOCUMENT NUMBER: 131:223488

TITLE: **Glutathione** analogs for modulation of hematopoiesis, mitigating the **bone marrow**-destructive effects of a chemotherapeutic agent, and potentiating the toxicity of chemotherapeutic agents

INVENTOR(S): Kauvar, Lawrence M.; Morgan, Amy S.; Lyttle, Matthew H.; Borch, Richard F.

PATENT ASSIGNEE(S): Terrapin Technologies, Inc., USA

SOURCE: U.S., 41 pp., Cont.-in-part of U.S. Ser. No. 636,516,

abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 18
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5955432	A	19990921	US 1996-675095	19960703
US 5599903	A	19970204	US 1993-126229	19930924
US 5786336	A	19980728	US 1994-305993	19940919
US 5767086	A	19980616	US 1995-482645	19950607

PRIORITY APPLN. INFO.: US 1992-863564 B2 19920403
US 1993-126229 A2 19930924
US 1994-305993 A2 19940919
US 1995-482645 A2 19950607
US 1996-636516 B2 19960419
US 1991-693245 B2 19910429
US 1993-130736 A2 19931001
OTHER SOURCE(S): MARPAT 131:223488
AB Compds. YCONHCH(CH2ZX)COG [YCO = .gamma.-Glu or .beta.-Asp; G = phenylGly, Gly; Z = CH2, O, S; X = C6-8 alkyl, arom. group], and the esters, amides, amide/esters and salts thereof, are useful in modulating hematopoiesis in **bone marrow**, mitigating the **bone-marrow**-destructive effects of a chemotherapeutic agent, and in potentiating the toxicity of chemotherapeutic agents.
REFERENCE COUNT: 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 19 OF 43 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:597711 HCAPLUS
DOCUMENT NUMBER: 132:218965
TITLE: Development of adverse reactions by whole-body x-ray irradiation and its prevention by antioxidant vitamins
AUTHOR(S): Saito, Shinichi; Sano, Mitsuaki
CORPORATE SOURCE: Hamamatsu Coll., Univ. Shizuoka, Japan
SOURCE: Tokubetsu Kenkyu Hokokusho - Shizuoka-kenritsu Daigaku Tanki Daigakubu (1999), Volume Date 1997 191-196
CODEN: TKTDFG; ISSN: 1340-2927
PUBLISHER: Shizuoka-kenritsu Daigaku Tanki Daigakubu
DOCUMENT TYPE: Journal
LANGUAGE: Japanese
AB Wistar rats were whole-body irradiated with x-ray, examd. changes of lipid peroxide, 4-hydroxy-2-nonenal, 4-hydroxy-2-nonenoic acid, antioxidant vitamins (E, C), 8-hydroxydeoxyguanosine in **bone marrow** cells and plasma, and compared with **glutathione** conjugate formation in controls.

L13 ANSWER 20 OF 43 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:272222 HCAPLUS
DOCUMENT NUMBER: 130:322369
TITLE: Influence of buthionine sulfoximine on radiation induced chromosome aberrations in mammalian cells

AUTHOR(S): Chattopadhyay, A.; Chatterjee, A.
CORPORATE SOURCE: Genetics Lab., Dep. Zoology, North-Eastern Hill Univ., Shillong, 793022, India
SOURCE: Schr. Forschungszent. Juelich, Bilateral Semin. Int. Bur. (1999), 30(Recent Aspects of Cellular and Applied Radiobiology), 89-92
CODEN: SFBBFA; ISSN: 1433-5581
PUBLISHER: Forschungszentrum Juelich GmbH
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Considering the parameters like DNA single strand breaks and cell survival, the radioprotective effect of cellular **glutathione** (GSH) has already been demonstrated in cells treated with buthionine sulfoximine (BSO), a potent GSH depleting agent. No report was available regarding the role of BSO on radiation induced chromosome aberrations (CAs) which reflects the influence of cellular GSH on radiation induced DNA double strand breaks. In this study the frequency of radiation induced CAs was found to increase except exchanges in BSO treated samples. The data indicate that free radical induced DNA lesions and low efficiency repair could be reasons for the obsd. increased sensitivity. GSH and GSH-ester post-treatment in samples irradiating at 4.degree. support the possible role of endogenous thiols including GSH in repair and misrepair processes on radiation induced DNA lesions.

REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 21 OF 43 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:149708 HCAPLUS
DOCUMENT NUMBER: 130:308509
TITLE: Radioprotective effects of 2-(allylthio)pyrazine an experimental chemopreventive agent: effects on detoxifying enzyme induction
AUTHOR(S): Kim, Sang Geon; Nam, Seon Young; Kim, Choon Won; Cho, Chul Koo; Kim, Nak Doo
CORPORATE SOURCE: College of Pharmacy, Duksung Women's University, Seoul, 132-714, S. Korea
SOURCE: Res. Commun. Mol. Pathol. Pharmacol. (1998), 101(3), 275-288
CODEN: RCMPE6; ISSN: 1078-0297
PUBLISHER: PJD Publications Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB 2-(Allylthio)pyrazine (2-AP), which is effective in suppressing constitutive and inducible cytochrome P 450 2E1 expression, exhibits hepatoprotective and chemopreventive effects. The radioprotective effects of 2-AP were examd. in animals in assocn. with the expression of microsomal epoxide hydrolase (mEH) and **glutathione** S-transferases (GSTs). 2-AP pretreatment (100 mg/kg/day, for 2 days) prior to total body irradn. (TBI) at the dose of 8 Gy increased the 30 day survival rate of mice to 91% from 48% in TBI alone. 2-AP caused an increase in the mean survival time of mice exposed to 9 Gy of TBI. Light microscopic examns. revealed that exposure of mice to 8 Gy of .gamma.-ray radiation resulted in hepatocyte degeneration in the surviving animals at day 1 through day 22 with certain extents of necrosis obsd. at early

times, whereas 2-AP pretreatment protected the liver against ionizing radiation with no hepatic necrosis being obsd. Mice irradiated at the dose of 8 Gy showed time-related decreases in the counts of WBC, RBC and platelet. 2-AP treatment, however, failed to protect the peripheral blood cells against .gamma.-irradn. and resulted in no improvement in the ratio of myeloid to erythroid **bone marrow** cells, as compared to TBI alone. Northern blot anal. revealed that exposure of mice to 8 Gy of TBI plus 2-AP exhibited greater mEH and mGSTA3 mRNA levels in the liver than those with TBI alone, although mGSTP1 mRNA level failed to be altered. Studies were also extended to det. the effects of 0.5 Gy .gamma.-irradn. in combination with 2-AP on the expression of hepatic mEH and GST genes in rats. Whereas mEH, rGSTA2, rGSTA3 and rGSTA5 mRNA levels were elevated 2- to 2.8-fold at 24 h after 2-AP treatment at the dose of 30 mg/kg, rats exposed to both 2-AP and 0.5 Gy of irradn. showed greater relative increases in the mRNAs. 2-AP enhanced the mEH and rGSTA2 gene expression to greater extents at day 1 after irradn. than after 3-5 consecutive daily treatment. The radiation-inducible mRNA levels of rGSTA3/5 and rGSTM1/2 were affected less by 2-AP pretreatment than were those of mEH and rGSTA2. These results demonstrate that 2-AP exhibits radioprotective efficacy against .gamma.-ray ionizing radiation in both mice and rats, which might be assocd. with enhanced expression of mEH and GST genes, but not with hematol. improvement.

REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 22 OF 43 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:625926 HCAPLUS
DOCUMENT NUMBER: 129:327775
TITLE: Protective effect of bismuth nitrate against injury to the **bone marrow** by .gamma.-irradiation in mice: possible involvement of induction of metallothionein synthesis
AUTHOR(S): Miura, Nobuhiko; Satoh, Masahiko; Imura, Nobumasa; Naganuma, Akira
CORPORATE SOURCE: Department of Molecular and Biochemical Toxicology, Faculty of Pharmaceutical Sciences, Tohoku University, Sendai, 980-8578, Japan
SOURCE: J. Pharmacol. Exp. Ther. (1998), 286(3), 1427-1430
CODEN: JPETAB; ISSN: 0022-3565
PUBLISHER: Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The effects of bismuth nitrate (BN) on the lethal effect of and injury to **bone marrow** by .gamma.-irradn. were examd. Mice were given daily s.c. injections of BN for 2 days and were exposed to whole-body irradn. (137Cs; 8 grays) 24 h after the second injection of BN. All mice exposed to .gamma.-irradn. without treatment with BN died within 30 days, but the lethal effect of .gamma.-irradn. was markedly reduced in mice given BN before irradn. Irradn. (3 grays) significantly reduced the total no. of leukocytes 1 day after irradn. but the no. of leukocytes subsequently increased in both nontreated and BN-treated irradiated mice. However, the rate of recovery of the total no. of leukocytes, as monitored from 5 days after irradn., was significantly higher in BN-treated mice than in the nontreated mice. Redns. in the viability of

hematopoietic stem **cells** (detd. by monitoring the no. of colony-forming units in the spleen) that were induced by .gamma.-irradn. (3 grays) were considerably diminished by the treatment of mice with BN before irradn. BN significantly increased the concn. of metallothionein in the **bone marrow** cells of mice, but levels of other cellular antioxidants, such as catalase, superoxide dismutase, **glutathione**-S-transferase, **glutathione** peroxidase and **glutathione**, were unchanged. These results suggest that BN protects **bone marrow** cells against the toxic effects of .gamma.-irradn. by inducing the synthesis of metallothionein in the **bone marrow**. Metallothionein might play an important role in detg. the sensitivity of animals to .gamma.-irradn.

L13 ANSWER 23 OF 43 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:403145 HCAPLUS
DOCUMENT NUMBER: 129:134868
TITLE: Extrathymic T cell deletion and allogeneic stem cell engraftment induced with costimulatory blockade is followed by central T cell tolerance
AUTHOR(S): Wekerle, Thomas; Sayegh, Mohamed H.; Hill, Joshua; Zhao, Yong; Chandraker, Anil; Sawenson, Kirsten G.; Zhao, Guiling; Sykes, Megan
CORPORATE SOURCE: Bone Marrow Transplant. Sect., Transplant. Biol. Res. Cent., Massachusetts General Hosp., Boston, MA, 02129, USA
SOURCE: J. Exp. Med. (1998), 187(12), 2037-2044
CODEN: JEMEAV; ISSN: 0022-1007
PUBLISHER: Rockefeller University Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A reliable,. nontoxic method of inducing transplantation tolerance is needed to overcome the problems of chronic organ graft rejection and immunosuppression-related toxicity. Treatment of mice with single injections of an anti-CD40 ligand antibody and CTLA4Ig, a low dose (3 Gy) of whole body irradn., plus fully major histocompatibility complex-mismatched allogeneic **bone marrow** transplantation (BMT) reliably induced high levels (>40%) of stable (>8 mo) multilineage donor hematopoiesis. Chimeric mice permanently accepted donor skin grafts (>100 d), and rapidly rejected third party grafts. Progressive deletion of donor-reactive host T cells occurred among peripheral CD4+ lymphocytes, beginning as early as 1 wk after **bone marrow** transplantation. Early deletion of peripheral donor-reactive host CD4 cells also occurred in thymectomized, similarly treated marrow recipients, demonstrating a role for peripheral clonal deletion of donor-reactive T cells after allogeneic BMT in the presence of costimulatory blockade. Central intrathymic deletion of newly developing T cells ensued after donor stem cell engraftment had occurred. Thus, we have shown that high levels of chimerism and systemic T cell tolerance can be reliably achieved without myeloablation or T cell depletion of the host. Chronic immunosuppression and rejection are avoided with this powerful, nontoxic approach to inducing tolerance.

L13 ANSWER 24 OF 43 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:289346 HCAPLUS

DOCUMENT NUMBER: 129:25134
TITLE: In vivo radioprotective effects of oltipraz in .gamma.-irradiated mice
AUTHOR(S): Kim, Sang Geon; Nam, Seon Young; Kim, Choon Won
CORPORATE SOURCE: College of Pharmacy, Duksung Women's University, Seoul, 132-714, S. Korea
SOURCE: Biochem. Pharmacol. (1998), 55(10), 1585-1590
CODEN: BCPCA6; ISSN: 0006-2952
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Previous studies in this lab. have shown that oltipraz (Olt), a chemopreventive agent, enhances radiation(Rad)-inducible **glutathione** S-transferase (GST) and microsomal epoxide hydrolase (mEH) expression in the liver. The present study was designed to investigate the in vivo radioprotective effect of Olt in ICR mice exposed to a LD of Rad. The 30-day survival rate of mice irradiated at the dose of 8 Gy was substantially increased to 91% by Olt pretreatment (100 mg/kg/day for 2 days), compared with 48% in animals irradiated alone. Light microscopic examns. revealed that exposure of mice to 8 Gy of .gamma.-ray Rad resulted in hepatocyte degeneration in the surviving animals from Day 1 through Day 22 after irradn. with certain degrees of necrosis obsd. at early times, whereas Olt treatment provided protection of the liver against irradn. with no hepatic necrosis noted. Mice irradiated at the dose of 8 Gy exhibited time-related decreases in the white blood cell (WBC), red blood cell (RBC), and platelet counts with maximal redn. noted at Day 10. Animals irradiated with Olt treatment showed no difference in peripheral blood cell counts or in the ratio of myeloid to erythroid **bone marrow** cells, compared with those irradiated alone. Northern RNA blot anal. showed that treatment of mice with Olt at the dose of 100 mg/kg in combination with 8 Gy irradn. resulted in 12-fold increases in hepatic mEH and mGSTA3 mRNA levels at 24-h post-treatment, whereas mGSTP1 mRNA levels were not altered. The mRNA levels for mEH and mGSTA3 were elevated after exposure of animals to both Olt and 8 Gy-.gamma. ray to a greater extent than after irradn. alone. The enhanced survival rate (91%) in 8 Gy-irradiated animals after treatment with Olt (100 mg/kg/day for 2 days) was completely reversed by concomitant pretreatment with dexamethasone (Dexa) (0.1 and 1 mg/kg/day for 2 days), a known inhibitor of mEH and GST expression, resulting in a 42% and 28% survival rate, resp. Mice irradiated after dexamethasone treatment at a dose of 1 mg/kg showed a reduced mean survival time compared with those treated with 0.1 mg/kg of dexamethasone (9 vs 14 days). The current study demonstrates that Olt is effective in increasing the survival rate of mice against ionizing Rad and that protective effects of Olt assocd. with enhanced expression of mEH and GST genes may represent its radioprotective efficacy.

L13 ANSWER 25 OF 43 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:72949 HCAPLUS
DOCUMENT NUMBER: 128:227987
TITLE: In vivo protection by cimetidine against fast neutron-induced micronuclei in mouse **bone marrow** cells
AUTHOR(S): Mozdarani, Hossein; Khoshbin-Khoshnazar, Ali R.

CORPORATE SOURCE: PO Box 14155-4838, School of Medical Sciences, Tarbiat Modarres University, Tehran, Iran
SOURCE: Cancer Lett. (Shannon, Irel.) (1998), 124(1), 65-71
CODEN: CALEDQ; ISSN: 0304-3835
PUBLISHER: Elsevier Science Ireland Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB We have previously shown that cimetidine is capable of reducing the clastogenic effect of .gamma.-rays. In this research the radioprotective property of this drug was examd. against low doses of fast neutrons using the micronucleus assay. Swiss albino male mice (12 wk old) were irradiated by fast neutrons emitted from a 241Am-9Be source. The absorbed doses were 1.5, 2.25, 3.375 and 5.06 cGy at a dose rate of 0.718 cGy/h. Two hours prior to neutron irradn. mice were treated by cimetidine at a concn. of 15 mg/kg body wt. injected i.p. Mice were sacrificed by cervical dislocation at different post-irradn. times (24, 48 and 72 h). The results obtained show that the frequency of neutron-induced micronuclei in polychromatic erythrocytes (PCEs) is significantly higher than those of control groups ($P<0.05$) at the neutron doses used in these expts. Moreover, cimetidine effectively reduced (1.5-2-fold) the frequency of micronuclei in PCE ($P<0.05$). These results show that cimetidine can protect **bone marrow** cells against clastogenic effects of low dose fast neutrons and hence high linear energy transfer (LET) radiation. The mechanism by which cimetidine reduces the clastogenic effects of fast neutrons is not fully understood. It might act through a free radical scavenging mechanism assocd. with the amplification of the **glutathione** system.

L13 ANSWER 26 OF 43 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:42294 HCAPLUS
DOCUMENT NUMBER: 128:124125
TITLE: Methods of promoting hematopoiesis using derivatives of human chorionic gonadotropin
INVENTOR(S): Gallo, Robert C.; Bryant, Joseph; Lunardi-Iskandar, Yanto
PATENT ASSIGNEE(S): University of Maryland Biotechnology Institute, USA; Gallo, Robert C.; Bryant, Joseph; Lunardi-Iskandar, Yanto
SOURCE: PCT Int. Appl., 175 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9749418	A1	19971231	WO 1997-US11209	19970624

W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE, GH, HU, IL, IS, JP, KG, KP, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, SL, TJ, TM, TR, TT, UA, US, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA,

GN, ML, MR, NE, SN, TD, TG

US 5968513	A	19991019	US 1996-709924		19960909
AU 9737924	A1	19980114	AU 1997-37924		19970624
PRIORITY APPLN. INFO.:			US 1996-669654	A2	19960624
			US 1996-709924	A2	19960909
			WO 1997-US11209	W	19970624

AB The present invention relates to methods of treating or preventing diseases or disorders assocd. with hematopoietic deficiency by administration of human chorionic gonadotropin, .beta.-human chorionic gonadotropin, a peptide contg. a sequence of one or more portions of .beta.-human chorionic gonadotropin, or fractions of a source of native human chorionic gonadotropin or native .beta.-human chorionic gonadotropin. The invention also relates to methods of treating and preventing diseases or disorders assocd. with hematopoietic deficiency by administration of **hematopoietic cells**, the nos. of which have been increased by contacting the cells with a therapeutic of the invention. Pharmaceutical compns. and methods of administration are also provided.

L13 ANSWER 27 OF 43 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:679106 HCAPLUS
DOCUMENT NUMBER: 127:336630
TITLE: Inhibitor and stimulator of stem cell proliferation and uses thereof
INVENTOR(S): Wolpe, Stephen D.; Tsyrlova, Irena
PATENT ASSIGNEE(S): Pro-Neuron, Inc., USA
SOURCE: PCT Int. Appl., 162 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9736922	A1	19971009	WO 1997-US5601	19970403
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5861483	A	19990119	US 1996-627173	19960403
CA 2249716	AA	19971009	CA 1997-2249716	19970403
AU 9724391	A1	19971022	AU 1997-24391	19970403
AU 727023	B2	20001130		
EP 891377	A1	19990120	EP 1997-920117	19970403
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
CN 1220670	A	19990623	CN 1997-195095	19970403
JP 2000508633	T2	20000711	JP 1997-535611	19970403
ZA 9802746	A	19990329	ZA 1998-2746	19980401

NO 9804628	A	19981201	NO 1998-4628		19981002
KR 2000005428	A	20000125	KR 1998-8185		19981002
PRIORITY APPLN. INFO.:			US 1996-627173	A	19960403
			US 1997-832443	A	19970403
			WO 1997-US5601	W	19970403

AB Disclosed and claimed are methods for the isolation and use of stem cell-modulating factors for regulating stem cell cycle and for accelerating the post-chemotherapy peripheral blood cell recovery. Also disclosed and claimed are inhibitors and stimulators of stem cell proliferation. Hb .alpha.-chain fragments are described that have the desired properties.

L13 ANSWER 28 OF 43 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:547405 HCAPLUS
DOCUMENT NUMBER: 127:160574
TITLE: The cytokine receptor WSX, agonist and antagonist ligands and their uses
INVENTOR(S): Bennett, Brian; Carter, Paul J.; Chiang, Nancy Y.; Kim, Kyung Jin; Matthews, William; Rodrigues, Maria L.
PATENT ASSIGNEE(S): Genentech, Inc., USA
SOURCE: PCT Int. Appl., 219 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9725425	A1	19970717	WO 1997-US325	19970107
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2241564	AA	19970717	CA 1997-2241564	19970107
AU 9715747	A1	19970801	AU 1997-15747	19970107
AU 721129	B2	20000622		
EP 885299	A1	19981223	EP 1997-901961	19970107
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2000503204	T2	20000321	JP 1997-525393	19970107
ZA 9700148	A	19980708	ZA 1997-148	19970108

PRIORITY APPLN. INFO.:	US 1996-585005	A	19960108
	US 1996-667197	A	19960620
	WO 1997-US325	W	19970107

AB The cytokine receptor WSX that plays a role in hematopoiesis is identified and antibodies to it (including agonist and neutralizing antibodies) are disclosed and uses for them are described. Uses for WSX ligands (e.g., anti-WSX receptor agonist antibodies or OB protein) in hematopoiesis are also disclosed. The gene for the receptor was cloned using probes derived

from a human liver expressed sequence tag to screen a Hep3B cDNA library and a full-length clone constructed from several overlapping clones. The receptor may play a role in control of cellular proliferation and it is expressed in fetus (lung, liver, kidney) and in adult (liver, placenta, lung, skeletal muscle, kidney, ovary, prostate, small intestine). A no. of variants of the receptor were found, of which one (13.2) was a receptor for OB protein (leptin). OB protein was found to interact synergistically with interleukin 3, stem cell factor, and GM-CSF in hematopoiesis with a preferential stimulation of myelopoiesis. The identification of agonist antibodies is described.

L13 ANSWER 29 OF 43 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:185729 HCAPLUS
DOCUMENT NUMBER: 126:235337
TITLE: Antioxidant effects of vitamin C in mice following x-irradiation
AUTHOR(S): Harapanhalli, Ravi S.; Yaghmai, Vahid; Giuliani, Dennis; Howell, Roger W.; Rao, Dandamudi V.
CORPORATE SOURCE: Dep. of Medicine, UMDNJ-New Jersey Medical Sch., Newark, NJ, 07103, USA
SOURCE: Res. Commun. Mol. Pathol. Pharmacol. (1996), 94(3), 271-287
CODEN: RCMPE6; ISSN: 1078-0297
PUBLISHER: PJD Publications
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The influence of supplemental vitamin C on the survival of nucleated **bone marrow** cells was examd. in Swiss Webster mice following whole-body sublethal x-irradn. (3.5 Gy). The vitamin protected these cells by a factor of 1.7 when cell count per tibia was taken as the biol. end point. However, in studies with lethal whole-body irradn. (9 Gy) and 30 day survival as the end point, supplemental ascorbic acid (AA) had no significant effect on the biol. outcome. Based on these studies, it appears that vitamin C is effective in protecting the nucleated cells at lower doses, but not at LDs. Studies on the mechanism of radioprotection by vitamin C at sublethal doses were carried out by following the response of endogenous AA and **glutathione** levels to x-irradn. (3.5 Gy) on mice fed with regular as well as vitamin C rich diet. The results suggest that (i) a **glutathione** controlled feedback mechanism regulates the plasma AA levels in mice; (ii) the role of vitamin C against radiation damage is not only in the initial stages of radical scavenging but also in cellular redox processes mediated by **glutathione**.

L13 ANSWER 30 OF 43 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:492724 HCAPLUS
DOCUMENT NUMBER: 125:189551
TITLE: Radioprotection of mice following garlic pretreatment
AUTHOR(S): Singh, SP; Abraham, SK; Kesavan, PC
CORPORATE SOURCE: School Life Sciences, Jawaharlal Nehru University, New Delhi, 110067, India
SOURCE: Br. J. Cancer, Suppl. (1996), 74(27), S102-S104
CODEN: BJCSB5; ISSN: 0306-9443
DOCUMENT TYPE: Journal

LANGUAGE: English

AB Freshly prepd. aq. ext. of garlic was tested in mice for its possible in vivo protective effect against gamma-radiation-induced chromosomal damage. In the same animals, the changes in the sulfydryl content and **glutathione** S-transferase activity were evaluated. Three doses of garlic ext. [125, 250 and 500 mg kg-1 body wt. (bw)] were administered orally for five consecutive days and the animals were exposed to 0.25, 0.5, 1.0 and 2.0 Gy gamma-radiation 2 h after the final feeding. The results of the **bone marrow** micronucleus test revealed that pretreatment with garlic ext. was effective in reducing gamma-radiation-induced chromosomal damage. Against 0.25 Gy gamma-radiation, a high dose of 500 mg kg-1 bw garlic ext. was required to significantly reduce the chromosomal damage. All the three doses of garlic ext. were effective in exerting a protective effect against 0.5, 1.0 and 2.0 Gy gamma-radiation. However a dose-related effect was obsd. only against 2.0 Gy. The sulphydryl content and **glutathione** S-transferase activity registered a significant increase after either pretreatment with garlic ext. or irradn. In the garlic ext. pretreated irradiated animals, a significant redn. was obsd. in the sulphydryl content and **glutathione** S-transferase activity.

L13 ANSWER 31 OF 43 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:363601 HCAPLUS
DOCUMENT NUMBER: 125:26256
TITLE: Stem cell proliferation inhibitors for use in the treatment of proliferative disorders
INVENTOR(S): Kozlov, Vladimir; Tsyrlova, Irena; Wolpe, Stephen D.
PATENT ASSIGNEE(S): Pro-Neuron, Inc., USA
SOURCE: PCT Int. Appl., 100 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9610634	A1	19960411	WO 1995-US12268	19950929
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TT				
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 6022848	A	20000208	US 1994-316424	19940930
US 5939391	A	19990817	US 1995-535882	19950928
AU 9537257	A1	19960426	AU 1995-37257	19950929
AU 712204	B2	19991028		
EP 784677	A1	19970723	EP 1995-935119	19950929
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 10509422	T2	19980914	JP 1995-511957	19950929
FI 9701000	A	19970528	FI 1997-1000	19970311
NO 9701444	A	19970526	NO 1997-1444	19970326

PRIORITY APPLN. INFO.:

US 1994-316424	A	19940930
US 1995-535882	A	19950928
US 1993-40924	A2	19930331
US 1993-40942	B2	19930331
WO 1994-US3349	A2	19940329
WO 1995-US12268	W	19950929

AB A reversible inhibitor of stem cell proliferation that inhibits the abnormal stem cell cycle and that is useful in the treatment of proliferative disease and in the support of chemotherapy for accelerating the post-chemotherapy peripheral blood cell recovery is purified and characterized. By controlling hyperproliferation, the immunosuppression assocd. with it is ameliorated. Methods for purifn. of the factor from **bone marrow** are described. The factor is purified from swine **bone marrow** and has a specific activity (IC50) of .ltoreq.20 ng/mL and a mol. wt. in the range 10-100 kilodaltons, and is hydrophobic and stable to heat and acid. Formulations using the factor in combination with Hb subunits for use in the support of chemotherapy are described. The biol. and therapeutic activity of the protein is demonstrated in in vitro and vivo systems.

L13 ANSWER 32 OF 43 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:355437 HCAPLUS
DOCUMENT NUMBER: 125:29252
TITLE: Mechanisms of protection by buthionine sulfoximine against .gamma.-ray-induced micronuclei in polychromatic erythrocytes of mouse **bone marrow**
AUTHOR(S): Sarma, Lakshmi; Devasagayam, T. P. A.; Mohan, Hari; Mittal, J. P.; Kesavan, P. C.
CORPORATE SOURCE: Biosciences Group, Bhabha Atomic Res. Centre, Bombay, 400 085, India
SOURCE: Int. J. Radiat. Biol. (1996), 69(5), 633-643
CODEN: IJRBE7; ISSN: 0955-3002
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The effect of pretreatment with buthionine sulfoximine (BSO) on the radiosensitivity of mouse **bone marrow** cells was studied using the in vivo micronucleus test. Varying concns. of BSO were injected into mice by i.p. injection 2 h before .gamma.-irradn., and the frequency of micronuclei in polychromatic erythrocytes (MnPCEs) of **bone marrow** were scored. Treatment with BSO resulted in a significant redn. (41% at 20 mg/kg body wt.) in the frequency of micronuclei induced by 1 Gy .gamma.-rays. Redn. was obsd. in cells sampled at 24, 30 and 48 h postirradn. with no apparent effect on the ratio of poly- to normochromatic erythrocytes in BSO-treated vs. control groups. **Glutathione** levels in the **bone marrow** of BSO-treated animals 2 h after a single injection were found to be unaltered. The protective effect of BSO was not obsd. if it was given either immediately or 2 h after irradn. Based on these and earlier findings it seemed as if BSO mols. may be involved in physicochem. reactions with reactive species generated in the system by irradn. BSO showed relatively high reaction rate consts. with hydroxyl radical (OH, 2.5 .times. 1019 dm3 mol-1 s1, calcd. on the basis on competition kinetics) and with singlet oxygen (1O2, 4.3 .times. 107 dm3 mol-1 s-1) but

a lower rate const. with hydrated electrons (.ltoreq.5.0 .times. 106 dm3 mol-1 s1). Based on half-life ests., transients formed and potential for damage to biomols., OH and 1O2 seemed to be the possible species responsible. In vitro studies reveal that BSO has significant abilities to protect DNA against single-strand breaks and lipid peroxidn. induced by 1O2 in microsomal membranes. This supports our hypothesis that BSO may be involved in scavenging the reactive species generated and that besides OH, 1O2 may also be a major payer in radiation damage.

L13 ANSWER 33 OF 43 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:153553 HCAPLUS
Correction of: 1995:571015
DOCUMENT NUMBER: 124:194319
Correction of: 122:306553
TITLE: Method of reducing or preventing **bone marrow** hypoplasia with L-2-oxothiazolidine-4-carboxylate
INVENTOR(S): Goldberg, Dennis I.; Pace, Gary; White, Randy D.; Wilson, Daniel M.
PATENT ASSIGNEE(S): Free Radical Sciences, Inc., USA
SOURCE: Can. Pat. Appl., 79 pp.
CODEN: CPXXEB
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CA 2124252	AA	19941129	CA 1994-2124252	19940525
US 5430045	A	19950704	US 1993-68385	19930528
PRIORITY APPLN. INFO.:			US 1993-68385	19930528
			US 1992-872549	19920423

AB A method for reducing, or preventing, **bone marrow** hypoplasia in a patient comprises administration of L-2-oxothiazolidine-4-carboxylate (I). To this end, when a **glutathione** intracellular stimulator, e.g. a virucide, is administered to such a patient, the risk of **bone marrow** hypoplasia is reduced or prevented. Mice were given twice daily 50-500 mg/kg AZT starting day 3 orally with feed and a diet contg. 1.0% I. Coadministration of I and AZT reduced some indexes of AZT-induced hematotoxicity.

L13 ANSWER 34 OF 43 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:47737 HCAPLUS
DOCUMENT NUMBER: 124:139959
TITLE: In vivo radioprotection with garlic extract
AUTHOR(S): Singh, S. P.; Abraham, Suresh K.; Kesavan, P. C.
CORPORATE SOURCE: School of Life Sciences, Jawaharlal Nehru University, New, DELHI-110067, India
SOURCE: Mutat. Res. (1995), 345(3,4), 147-53
CODEN: MUREAV; ISSN: 0027-5107
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Garlic ext. was evaluated in the mouse **bone marrow**

micronucleus test for its possible protective effects against .gamma.-ray-induced chromosomal damage. Together with this, biochem. assays were carried out to det. the changes in sulfhydryl content and **glutathione** S-transferase activities. Three doses of freshly prepd. garlic ext. (125, 250 and 500 mg/kg b.w.) were orally administered for 5 consecutive days, and the animals were irradiated 2 h after the final feeding. The results of the micronucleus test demonstrated that pre-treatment with garlic ext. can lead to significant dose-related redns. in the frequencies of .gamma.-ray-induced (2 Gy) micronucleated polychromatic erythrocytes. The anticlastogenic effect of garlic ext. was obsd. against lower radiation doses of 0.5 and 1 Gy, but not 0.25 Gy. Significant increases in the sulfhydryl content and **glutathione** S-transferase activity were obsd. after either pre-treatment with garlic ext. or irradn. However, the irradiated garlic-ext. pre-treated animals showed a significant redn. in sulfhydryl content and **glutathione** S-transferase activities.

L13 ANSWER 35 OF 43 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:571015 HCAPLUS
DOCUMENT NUMBER: 122:306553
TITLE: Method of reducing or preventing **bone marrow** hypoplasia with L-2-oxothiazolidine-4-carboxylate
INVENTOR(S): Goldberg, Dennis I.; Pace, Gary; White, Randy D.; Wilson, Daniel M.
PATENT ASSIGNEE(S): Free Radical Sciences, Inc., USA
SOURCE: Can. Pat. Appl., 79 pp.
CODEN: CPXXEB
DOCUMENT TYPE: Patent
LANGUAGE: English
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CA 2124252 AA		19941129	CA 1994-2124252	19940525
PRIORITY APPLN. INFO.:			US 1993-68385	19930528

AB A method for reducing, or preventing, **bone marrow** hypoplasia in a patient comprises administration of L-2-oxothiazolidine-4-carboxylate (I). To this end, when a **glutathione** intracellular stimulator, e.g. virucides, is administered to such a patient, the risk of **bone marrow** hypoplasia is reduced or prevented. Mice were given twice daily 50-500 mg/kg AZT starting day 3 orally with feed and a diet contg. 1.0% I. Coadministration of I and AZT reduced some indexes of AZT-induced hematotoxicity.

L13 ANSWER 36 OF 43 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:235626 HCAPLUS
DOCUMENT NUMBER: 122:26864
TITLE: Effect of .beta.-carotene on spontaneous and x-ray-induced chromosomal damage in **bone marrow** cells of mice
AUTHOR(S): Umegaki, Keizo; Takeuchi, Nozomi; Ikegami, Sachie; Ichikawa, Tomio
CORPORATE SOURCE: National Institute of Health and Nutrition, Tokyo,

162, Japan
SOURCE: Nutr. Cancer (1994), 22(3), 277-84
CODEN: NUCADQ; ISSN: 0163-5581
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The effect of .beta.-carotene on spontaneous and X-ray-induced chromosomal damage in **bone marrow** cells of mice was studied. As a source of .beta.-carotene, dried Dunaliella bardawil (contg. 6% .beta.-carotene) or oil suspension of Dunaliella .beta.-carotene was used. In Expt. 1, mice were given a basal diet, a 0.5% Dunaliella diet, or a 4% Dunaliella diet for four weeks. In Expt. 2, mice were given an oil suspension of Dunaliella .beta.-carotene (300 mg/kg body wt) by gavage for seven days while being fed a fat-rich diet. After .beta.-carotene treatment for the indicated time, spontaneous and X-ray (0.3 Gy, whole-body)-induced chromosomal damage in **bone marrow** cells was evaluated in terms of the percentages of micronucleated reticulocytes in their peripheral blood. The .beta.-carotene treatment slightly lowered the spontaneous and X-ray-induced chromosomal damage in **bone marrow** cells. Despite the higher doses of .beta.-carotene, the concns. of .beta.-carotene in **bone marrow**, liver, and serum were much lower than those of vitamin E. In addn., the .beta.-carotene treatment markedly lowered the concn. of vitamin E in the tissues.

L13 ANSWER 37 OF 43 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1994:211600 HCAPLUS
DOCUMENT NUMBER: 120:211600
TITLE: Modulation by bryostatin 1 of the in vitro radioprotective effects of the GM-CSF/IL-3 **fusion protein**, PIXY 321, on normal human myeloid progenitors
AUTHOR(S): Grant, Steven; Traylor, Rebecca; Pettit, George R.; Lin, Peck Sun
CORPORATE SOURCE: Div. Hematol./Oncol., Med. Coll. Virginia, Richmond, VA, 23298, USA
SOURCE: Cytokine (Philadelphia) (1993), 5(5), 490-7
CODEN: CYTIE9; ISSN: 1043-4666
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The authors have examd. the effect of the macrocyclic lactone PK-C activator, bryostatin 1, on the in vitro radioprotective capacity of the GM-CSF/IL-3 **fusion protein**, PIXY 321, toward normal committed myeloid progenitors (day 14 CFU-GM). Preincubation of CD 34+ cells for 24 h with 10 ng/mL PIXY 321 exerted significant radioprotective effects on these progenitors, (D = 1.403 vs 0.715 for controls), which were at least as great as those previously reported for higher concns. (e.g., 50 ng/mL) or rGM-CSF. In contrast to the results of earlier studies involving rGM-CSF, preincubation of cells with both PIXY 321 and 10 nM bryostatin 1 did not lead to an increase in radioprotective effect when the total no. of day 14 colonies was assessed. However, combinations of PIXY 321 and bryostatin 1 (or the tumor-promoting PK-C activator, PDBu) significantly increased the relative percentage and abs. no. of surviving non-eosinophilic colonies (e.g., pure neutrophil, pure monocyte-macrophage, or mixed neutrophil-macrophage) at each radiation

dose level. A similar pattern of response was noted in cells irradiated without a preconditioning interval, and in cells exposed to divided radiation doses. These results indicate that the GM-CSF/IL-3 **fusion protein** PIXY 321 exhibits significant in vitro radioprotective effects toward normal human **bone marrow** myeloid progenitors, and that co-administration of PK-C activators such as bryostatin 1 or PDBu selectively augments the radioprotective capacity of this hybrid cytokine toward non-eosinophilic elements.

L13 ANSWER 38 OF 43 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1994:95750 HCAPLUS
DOCUMENT NUMBER: 120:95750
TITLE: Method and recombinant cells for providing increased resistance of **hematopoietic** progenitor **cells** to toxicity of chemotherapeutic agents
INVENTOR(S): Hamilton, Thomas C.; Godwin, Andrew K.; Meister, Alton; Anderson, Mary E.; Huang, Chin Shiou
PATENT ASSIGNEE(S): Fox Chase Cancer Center, USA; Cornell Research Foundation, Inc.
SOURCE: PCT Int. Appl., 41 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9320195	A1	19931014	WO 1993-US2929	19930330
W: AU, CA, JP				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9339699	A1	19931108	AU 1993-39699	19930330
PRIORITY APPLN. INFO.:			US 1992-862525	19920401
			WO 1993-US2929	19930330

AB Methods and recombinant cells are provided for increasing the resistance of **hematopoietic** progenitor **cells** to the toxic effect of chemotherapeutic and other therapeutic agents used in treating tumors and malignancies. **Hematopoietic** progenitor **cells** are obtained from **bone marrow** donors. The cells are genetically altered by introduction, and stable incorporation into the genome, of .gtoreq.1 DNA encoding a protein capable of increasing intracellular **glutathione** prodn., thereby imparting to the cells the capability of producing increased amts. of intracellular **glutathione**. The altered cells are introduced into a patient for whom chemotherapy has been prescribed. The patient may then be treated with dosages of chemotherapeutic agents that would be toxic to the nonrecombinant cells. CDNA encoding .gamma.-glutamylcysteine synthetase was transfected and expressed in cultured ovarian cancer cells.

L13 ANSWER 39 OF 43 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1993:485597 HCAPLUS
DOCUMENT NUMBER: 119:85597
TITLE: Changes in plasma amino acids during conditioning therapy prior to **bone marrow**

transplantation: their relevance to antioxidant status
AUTHOR(S): Hunnisett, A. G.; Kars, A.; Howard, J. M. H.; Davis, S.
CORPORATE SOURCE: Biolab Med. Unit, London, UK
SOURCE: Amino Acids (1993), 4(1-2), 177-85
CODEN: AACIE6
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Amino acid metab. and oxidant status in **bone marrow** transplant (BMT) recipients was investigated before and after conditioning therapy. The conditioning therapy consisted of various combinations of cyclophosphamide, daunorubicin, cytosine arabinoside, idarubicin, vincristine, tenoposide, prednisolone, BCNU, and/or total body irradn. A marked decrease in the plasma concn. of a no. of amino acids, esp. those concerned with antioxidants, was obsd. over the 7 days of conditioning therapy. There was also a significant redn. in antioxidant capability, as reflected by measurements of **glutathione** and erythrocyte **glutathione** peroxidase, which may have an influence on post-transplant recovery and graft function. Such a redn. in antioxidant concns. may also have an effect on the erythrocyte and platelet support required post-grafting. The data presented adds to the evidence for the conditional essentiality of some amino acids such as taurine and glutamine, and may support the case for specific antioxidant intervention treatment prior to, and/or after conditioning therapy together with monitoring antioxidant status during the post-grafting period.

L13 ANSWER 40 OF 43 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1991:224576 HCAPLUS
DOCUMENT NUMBER: 114:224576
TITLE: Interleukin 1 alpha stimulates hemopoiesis but not tumor cell proliferation and protects mice from lethal total body irradiation
AUTHOR(S): Constine, L. S.; Harwell, S.; Keng, P.; Lee, F.; Rubin, P.; Siemann, D.
CORPORATE SOURCE: Med. Cent., Univ. Rochester, Rochester, NY, 14642, USA
SOURCE: Int. J. Radiat. Oncol., Biol., Phys. (1991), 20(3), 447-56
CODEN: IOBPD3; ISSN: 0360-3016
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Interleukin 1 alpha (IL-1) is a polypeptide/glycoprotein growth factor with multiple functions including the modulation of **hematopoietic cell** proliferation and differentiation. In vivo studies were performed with C57BL/6J mice injected with 0, 0.2, or 2.0 .mu.g of IL-1 24 h before or after lethal total-body .gamma.-irradn. (TBI) (9.5 Gy). More mice in the groups administered IL-1 before TBI survived (90% of the 2.0 .mu.g group) than those treated 2 or 24 h after TBI, which was still slightly superior to the uninjected group, which all died within 15 days. Proliferation of **bone marrow** granulocyte/macrophage colonies following split dose TBI was also greatest for mouse groups treated with IL-1 prior to TBI. These expts. support data from other investigators that IL-1 stimulation of BM is related to IL-1 timing with respect to TBI. Stimulation of hemopoiesis was also assessed in terms of changes in peripheral blood and BM cell nos. and cell cycle kinetics using

an electronic particle counter and flow cytometric techniques. Mice injected with 2 .mu.g of IL-1 showed an initial decline (at 3-6 H) and then a selective proliferation (24-48 h) of early and more committed progenitor cells to 125% and 200% of control values, resp. Peripheral blood counts rose accordingly. Cells in S and G2/M phases increased over 10 h and then declined in no. It thus appeared that some synchronization of cell cycling occurred, which might place cells in a more radioresistant phase of the cell cycle. The **glutathione** (GSH) content and synthesis in BM cells were measured by isocratic paired-ion HPLC and [35S]cysteine incorporation into the GSH tripeptide. An increase in cellular GSH content and synthesis was demonstrated following IL-1 which lasted 24 h, suggesting a possible mechanism for the radioprotection by IL-1. To det. the potential for achieving a favorable therapeutic ratio, KHT tumor-bearing mice were injected with 2.0 .mu.g IL-1. No change in tumor diams. or wts. or tumor cell clonogenicity between IL-1 treated or untreated animals was obsd. These expts. strongly support a role for IL-1 in stimulating **bone marrow** to overcome the myelosuppressive effects of irradn.

L13 ANSWER 41 OF 43 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1989:150537 HCAPLUS
DOCUMENT NUMBER: 110:150537
TITLE: Protection against ionizing radiation by combinations of radioprotectors
AUTHOR(S): Maisin, Jean R.
CORPORATE SOURCE: Biol. Dep., Cent. Etud. Energ. Nucl., Mol, B-2400, Belg.
SOURCE: Pharmacol. Ther. (1988), 39(1-3), 189-93
CODEN: PHTHDT; ISSN: 0163-7258
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The radioprotective efficacy of AET, GSH, 5-HT, cytosine, cysteamine, mannozime, and GLP/BO4 (unbranched glucans with alternating .beta.-1,3 and .beta.-1,6 bands having a N content of 1.9% and P content of 3.8%) was studied in mice when used in mixts. of .gtoreq.2 compds. A combination of sulfhydryl compds. did not markedly enhance the 30-day survival but the combinations decreased toxicity of the most active radioprotectants, such as AET. The most potent radioprotective mixt. consisted of a mixt. of AET, GSH, cysteine, cysteamine, and 5-HT, which yielded a dose redn. factor of 2.8 compared to 1.7 for AET, 5-HT, or cysteamine alone. Treatment with isogenic **bone marrow** increased survival with this combined treatment even more (dose redn. factor .gtoreq.3.7). The efficacies of radioprotection afforded by other combination treatments with respect to other biol. end-points, e.g., gastrointestinal syndrome, hematopoiesis, are discussed.

L13 ANSWER 42 OF 43 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1988:563111 HCAPLUS
DOCUMENT NUMBER: 109:163111
TITLE: Beneficial effect of muroctasin on experimental leukopenia induced by cyclophosphamide or irradiation in mice
AUTHOR(S): Nakajima, R.; Ishida, Y.; Yamaguchi, F.; Otani, T.; Ono, Y.; Nomura, M.; Une, T.; Osada, Y.

CORPORATE SOURCE: Res. Inst., Daiichi Seiyaku Co., Ltd., Tokyo, 134, Japan
SOURCE: Arzneim.-Forsch. (1988), 38(7A), 986-92
CODEN: ARZNAD; ISSN: 0004-4172
DOCUMENT TYPE: Journal
LANGUAGE: English

AB S.c. injection of muroctasin (I), a synthetic muramyl dipeptide deriv., favored recovery of mice from exptl. leukopenia induced by cyclophosphamide or by irradn. with X-rays. These effects were obsd. only when I treatment occurred after cyclophosphamide injection or X-ray irradn. Prophylactic treatment resulted in neither preventive nor restorative efficacy on leukopenia. In contrast, **glutathione** was hardly effective on leukopenia in both models, irresp. of treatment timing. The restorage efficacy of I was dose-dependent and attributable at least to its augmenting effect on colony-stimulating factor prodn., followed by the marked proliferation and differentiation of myeloblasts towards mature granulocytes in the **bone marrow**. These beneficial effects of I warrant further evaluation of its clin. usefulness in protecting against side effects of anticancer drugs and radiotherapy.

L13 ANSWER 43 OF 43 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1987:15190 HCAPLUS
DOCUMENT NUMBER: 106:15190
TITLE: Role of endogenous **glutathione** in realization of the oxygen effect in **bone marrow** cells
AUTHOR(S): Konstantinova, M. M.; Dontsova, G. V.; Smirnova, I. B.; Rakhmanina, O. N.
CORPORATE SOURCE: N. K. Kol'tsov Inst. Dev. Biol., Moscow, USSR
SOURCE: Radiobiologiya (1986), 26(5), 674-7
CODEN: RADOA8; ISSN: 0033-8192
DOCUMENT TYPE: Journal
LANGUAGE: Russian

AB The possible role of GSH in the radioprotective effect of hypoxia was investigated with 2 different cell types, Ehrlich ascites carcinoma cells and hemopoietic **bone marrow** cells. In both cell types, hypoxia induced an increase in GSH. Redn. of the GSH in the hypoxic cells by treatment with N-ethylmaleimide caused a corresponding decrease in radioprotection. Thus, a role for GSH in the radioprotective effect of hypoxia was demonstrated.

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show files
File 155:MEDLINE(R) 1966-2002/Jan W2
File   5:Biosis Previews(R) 1969-2002/Jan W4
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File  10:AGRICOLA 70-2002/Jan
         (c) format only 2002 The Dialog Corporation
File  34:SciSearch(R) Cited Ref Sci 1990-2002/Feb W1
         (c) 2002 Inst for Sci Info
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         (c) 2002 The HW Wilson Co
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         (c) 2002 The Gale Group
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File 357:Derwent Biotechnology Abs 1982-2002/Feb B1
         (c) 2002 Derwent Publ Ltd
File 434:SciSearch(R) Cited Ref Sci 1974-1989/Dec
         (c) 1998 Inst for Sci Info
File 440:Current Contents Search(R) 1990-2002/Feb W1
         (c) 2002 Inst for Sci Info
?ds

Set     Items   Description
S1       2741   ((CARRIER OR MALTOSE(W)BINDING)(W)(PEPTIDE? OR PROTEIN?) OR
             GLUTATHIONE(2W)TRANSFERASE? OR HIS(2W)HIS(2W)HIS(2W)HIS(2W)H-
            IS(2W)HIS) AND (BONE(W)MARROW OR HEMOPOIE? OR LIN OR CD34?)
S2       1833   RD (unique items)
S3        123   S2 AND FUSION(W)(PEPTIDE? OR PROTEIN?)
S4          0   S3 AND (VASOSTATIN OR CALRETICULUM OR COLLECTIN)
S5          2   S2 AND (VASOSTATIN OR CALRETICULUM OR COLLECTIN)
S6          2   S2 AND (VASOSTATIN OR CALRETULIN OR COLLECTIN)
S7          2   S2 AND (VASOSTATIN OR CALRETICULIN OR COLLECTIN)
S8          2   S5 OR S6 OR S7
S9         25   S2 AND (CHEMOTHERAP? OR RADIATION  OR RADIOTHERAP?)(5N)TOX-
              IC?
?t9/3 ab/1-25
>>>No matching display code(s) found in file(s): 65

 9/AB/1     (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09628078   98043304   PMID: 9382956
   Fibronectin fragment-facilitated retroviral transfer of the  glutathione
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-S- transferase pi gene into CD34 + cells to protect them against alkylating agents.

Kuga T; Sakamaki S; Matsunaga T; Hirayama Y; Kuroda H; Takahashi Y; Kusakabe T; Kato I; Niitsu Y

4th Department of Internal Medicine, Sapporo Medical University School of Medicine, Japan.

Human gene therapy (UNITED STATES) Nov 1 1997, 8 (16) p1901-10, ISSN 1043-0342 Journal Code: A12

Languages: ENGLISH

Document type: Journal Article

Record type: Completed

To protect bone marrow cells from the toxicity of chemotherapy , a multidrug resistant gene or a dihydrofolate reductase gene has been introduced into stem cells. These genes, however, are not capable of conferring refractoriness to alkylating agents (AA), which are some of the most commonly used agents in chemotherapy regimens. In the present study, an attempt was made to endow human stem cell (CD34 + cells) with resistance to cyclophosphamide, a well-known AA, and adriamycin (ADM) by transducing the glutathione -S- transferase pi (GST-pi) gene whose product is thought to detoxify AA by conjugating them with glutathione and to remove a toxic peroxide formed by ADM. The gene transduction was carried out retrovirally with a virus titer of 1 x 10(5) FFU/ml, employing a recombinant fibronectin fragment; transduction efficiency was extremely low without the fragment. Incubation with interleukin-6 and stem cell factor enhanced the expression of fibronectin ligands VLA4 and VLA5 on CD34 + cells. This enhanced expression of VLA4 and VLA5 was considered to facilitate a close contact of the CD34 + cell to the retroviral vector via fibronectin fragments and the subsequent transduction process. The GST-pi gene-transduced CD34 + cells formed almost 3- and 2.5-fold more CFU-GM than neo gene-transduced CD34 + cells in the presence of 2.5 microg/ml of 4-hydroperoxycyclophosphamide (4-HC), an active form of cyclophosphamide, and 30 ng/ml ADM, respectively. The transfectants formed an appreciable number of colonies, even at higher concentrations of these drugs (5.0 microg/ml of 4-HC, 50 ng/ml of ADM) whereas neo gene-transduced or nontransduced CD34 + cells formed no colonies at all, indicating the possibility of selecting out the transfectants by exposing them to these anticancer drugs. Thus, we were able to demonstrate that transduction of the GST-pi gene confers resistance to cyclophosphamide as well as to ADM, and therefore this approach can be applied clinically for high-dose chemotherapy.

9/AB/2 (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09325447 97246187 PMID: 9090786

In vivo drug-selectable genes: a new concept in gene therapy.

Licht T; Herrmann F; Gottesman MM; Pastan I

Laboratory of Molecular Biology, National Cancer Institute, Bethesda, Maryland 20892-4255, USA.

Stem cells (UNITED STATES) 1997, 15 (2) p104-11, ISSN 1066-5099 Journal Code: BN2

Languages: ENGLISH

Document type: Journal Article; Review; Review, Tutorial

Record type: Completed

Chemoresistance genes, initially considered to be a major impediment to the successful treatment of cancer, may become useful tools for gene therapy of cancer and of genetically determined disorders. Various target cells are rendered resistant to anticancer drugs by transfer of chemoresistance genes encoding P-glycoprotein, the multidrug resistance-associated protein-transporter, dihydrofolate reductase,

glutathione -S- transferase , O6-alkylguanine DNA alkyltransferase, or aldehyde reductase. These genes can be used for selection in vivo because of the pharmacology and pharmacokinetics of their substrates. In contrast, several other selectable marker genes conferring resistance to substrates like neomycin or hygromycin can only be utilized in tissue culture. Possible applications for chemoresistance genes include protection of bone marrow and other organs from adverse effects caused by the toxicity of chemotherapy . Strategies have also been developed to introduce and overexpress nonselectable genes in target cells by cotransduction with chemoresistance genes. Thereby expression of both transgenes can be increased following selection with drugs. Moreover, treatment with chemotherapeutic agents should restore transgene expression when or if expression levels decrease after several weeks or months. This approach may improve the efficacy of somatic gene therapy of hematopoietic disorders which is hampered by low or unstable gene expression in progenitor cells. In this article we review preclinical studies in tissue culture and animal models, and ongoing clinical trials on transfer of chemoresistance genes to hematopoietic precursor cells of cancer patients.

9/AB/3 (Item 3 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

05878058 86130738 PMID: 3511917
Enzymatic defense against radiation damage in mice. Effect of selenium and vitamin E depletion.
Batist G; Reynaud A; Katki AG; Travis EL; Shoemaker MC; Greene RF; Myers CE
Biochemical pharmacology (ENGLAND) Feb 15 1986, 35 (4) p601-6, ISSN 0006-2952 Journal Code: 9Z4
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Radiation effects are mediated in part by the generation of oxygen-derived free radicals and hydrogen peroxide. Membrane polyunsaturated fatty acids are important biological targets of these toxic molecules which cause lipid peroxidation. Radiation damage to DNA is also known to result in base hydroperoxides, especially thymidine hydroperoxide. Glutathione (GSH) is known to inhibit lipid peroxidation both chemically and through its interaction with the selenium-dependent glutathione peroxidase (GSH-Px). Although cytosolic GSH-Px can metabolize organic lipid peroxides in solution, it cannot metabolize phospholipid peroxides in micelles. This may be due to the interference of phase differences between the aqueous cytosol and the membrane, or the result of steric hindrance. Recent studies have suggested the presence of a membrane-bound GSH-dependent peroxidase system. We examined the cytosolic versus membrane-associated GSH-Px, in various tissues of mice on a selenium and vitamin E deficient diet, and found significant differences among organs in the distribution of enzyme activity in these two subcellular fractions. The effect of single high-dose whole body irradiation did not appear to be related to the activity of these enzymes.

9/AB/4 (Item 1 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

12007858 BIOSIS NO.: 199900288377
Improving enzymes for cancer gene therapy.
AUTHOR: Encell Lance P; Landis Daniel M; Loeb Lawrence A(a)
AUTHOR ADDRESS: (a)Joseph Gottstein Memorial Cancer Research Laboratory,

Departments of Pathology and Biochemistry,**USA
JOURNAL: Nature Biotechnology 17 (2):p143-147 Feb., 1999
ISSN: 1087-0156
DOCUMENT TYPE: Literature Review
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English

ABSTRACT: New techniques now make it feasible to tailor enzymes for cancer gene therapy. Novel enzymes with desired properties can be created and selected from vast libraries of mutants containing random substitutions within catalytic domains. In this review, we first consider genes for the ablation of tumors, namely, genes that have been mutated (or potentially can be mutated) to afford enhanced activation of pro-drugs and increased sensitization of tumors to specific chemotherapeutic agents. We then consider genes that have been mutated to provide better protection of normal host tissues, such as bone marrow , against the toxicity of specific chemotherapeutic agents. Expression of the mutant enzyme could render sensitive tissues, such as bone marrow , more resistant to specific cytotoxic agents.

1999

9/AB/5 (Item 2 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

10372426 BIOSIS NO.: 199698827344
Levels of antioxidants in haemolysates from breast cancer patients after chemo- and radiotherapy.
AUTHOR: Singh W Vasigara; Subramaniam S; Subramaniam Shyama; Devi C S Shyamala(a)
AUTHOR ADDRESS: (a)62, Second Main Road, Gandhi Nagar, Adyar, Madras - 600 020, Tamil Nadu**India
JOURNAL: Medical Science Research 24 (3):p195-197 1996
ISSN: 0269-8951
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Treatment with CMF (cyclophosphamide, methotrexate and 5-fluorouracil) and radiation (RT) produce severe side effects such as intestinal toxicity, bone - marrow depression, pneumotoxicity and cardiotoxicity. The main aim of this study is to determine the mechanism of toxicity and then alleviate it. The toxicities in CMF, radiation and CMF plus radiation treated breast cancer patients were signified by the levels of increased malonyldialdehyde in serum, erythrocytes and erythrocyte membranes. The levels of antioxidant glutathione and antioxidant enzymes such as superoxide dismutase, catalase and glutathione -s- transferase were decreased. The decrease in the activities of antioxidant enzymes might be due to the release of CMF metabolites which bind directly to the -SH groups, resulting in the lowering of the antioxidant enzyme activities. Radiation also produces free radicals and decreases the activity of antioxidant enzymes. Hence in this study, the supplementation of an antioxidant which can protect the -SH group and thereby alleviate the CMF+RT induced toxicities is attempted.

1996

9/AB/6 (Item 3 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

09694395 BIOSIS NO.: 199598149313
Glutathione -S- transferase expression in mammary tumours and bone marrow cells.
AUTHOR: Schecter R L; Cournoyer D; Batist G(a)
AUTHOR ADDRESS: (a)Dep. Med., Jewish Gen. Hosp., McGill Univ., 3755 Cote-Ste-Catherine Rd., Montreal, PQ H3T 1E2**Canada
JOURNAL: Cellular Pharmacology 1 (4):p153-157 1994
ISSN: 1351-3214
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: The glutathione -S- transferase (GST) isozyme encoding genes have been classified into multigene families (alpha, mu, pi) based on nucleotide sequence homology. These isozymes appear to play an important role in cellular defense against toxic chemicals including chemotherapeutic drugs. Both tissue and species-specific expression of the various GST forms have been observed. In this study, we have examined GST expression in rodent and human malignant mammary tissue and normal bone marrow . The latter is commonly the dose-limiting organ for systemic chemotherapy. Both mouse and rat mammary tumour tissue expressed alpha class GST; in addition, the rat tissue expressed the pi class subunit. We have also examined GST isozyme composition in human and rat bone marrow and have found expression of both alpha and pi class GST in these tissues. GST enzyme activity measurements revealed that human marrow has a sixfold higher level of activity relative to rat bone marrow . The information obtained in this study will be instrumental in planning therapeutic strategies to modulate GST activity to overcome drug resistance or to confer drug protection to dose-limiting organs such as the bone marrow by retroviral gene transfer of GST isozymes.

1994

9/AB/7 (Item 1 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

05389938 Genuine Article#: VV278 Number of References: 112
Title: CHEMOPROTECTION OF NORMAL-TISSUES BY TRANSFER OF DRUG-RESISTANCE GENES (Abstract Available)
Author(s): RAFFERTY JA; HICKSON I; CHINNASAMY N; LASHFORD LS; MARGISON GP; DEXTER TM; FAIRBAIRN LJ
Corporate Source: CHRISTIE HOSP NHS TRUST,PATERSON INST CANC RES,CRC DEPT CARCINOGENESIS/MANCHESTER M20 9BX/LANCS/ENGLAND/; CHRISTIE HOSP NHS TRUST,PATERSON INST CANC RES,CRC DEPT EXPT HAEMATOL/MANCHESTER M20 9BX/LANCS/ENGLAND/
Journal: CANCER AND METASTASIS REVIEWS, 1996, V15, N3 (SEP), P365-383
ISSN: 0167-7659
Language: ENGLISH Document Type: REVIEW
Abstract: The effectiveness of many types of antitumour agent is limited by (i) acute dose limiting cytotoxicity, principally myelosuppression but also lung, liver and gastrointestinal tract toxicity, (ii) the risk of therapy related secondary malignancy and (iii) the inherent or acquired drug-resistance of tumour cells. As the management of the acute toxic effects improve, the more insidious effects, and particularly

haematological malignancies, are anticipated to increase. Furthermore, attempts to overcome tumour cell resistance to treatment can lead to increased collateral damage in normal tissues.

One approach to circumventing both the acute toxic and chronic carcinogenic effects of chemotherapy would be to use gene therapy to achieve high levels of expression of drug resistance proteins in otherwise drug-sensitive tissues. To date the products of the multi-drug resistance (MDR-1) and the human O-6-alkylguanine-DNA-alkyltransferase (ATase) gene have been used in preclinical experiments to demonstrate proof of principle, and the former of these is now being tested in a clinical situation.

Here we discuss the potential of drug-resistance gene therapy to provide chemoprotection to normal tissues and examine the prospects for a dual approach which combines this with pharmacological sensitisation of tumours to chemotherapeutic agents.

9/AB/8 (Item 2 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

04759651 Genuine Article#: UF457 Number of References: 22
Title: LEVELS OF ANTIOXIDANTS IN HEMOLYSATES FROM BREAST-CANCER PATIENTS AFTER CHEMOTHERAPY AND RADIOTHERAPY (Abstract Available)
Author(s): SINGH WV; SUBRAMANIAM S; SUBRAMANIAM S; DEVI CSS
Corporate Source: UNIV MADRAS,DEPT BIOCHEM/MADRAS 600025/TAMIL NADU/INDIA/; UNIV MADRAS,DEPT BIOCHEM/MADRAS 600025/TAMIL NADU/INDIA/
Journal: MEDICAL SCIENCE RESEARCH, 1996, V24, N3 (MAR), P195-197
ISSN: 0269-8951
Language: ENGLISH Document Type: ARTICLE
Abstract: Treatment with CMF (cyclophosphamide, methotrexate and 5-fluorouracil) and radiation (RT) produce severe side effects such as intestinal toxicity, bone - marrow depression, pneumotoxicity and cardiotoxicity. The main aim of this study is to determine the mechanism of toxicity and then alleviate it. The toxicities in CMF, radiation and CMF plus radiation treated breast cancer patients were signified by the levels of increased malonyldialdehyde in serum, erythrocytes and erythrocyte membranes. The levels of antioxidant glutathione and antioxidant enzymes such as superoxide dismutase, catalase and glutathione -s- transferase were decreased. The decrease in the activities of antioxidant enzymes might be due to the release of CMF metabolites which bind directly to the -SH groups, resulting in the lowering of the antioxidant enzyme activities. Radiation also produces free radicals and decreases the activity of antioxidant enzymes. Hence in this study, the supplementation of an antioxidant which can protect the -SH group and thereby alleviate the CMF+RT induced toxicities is attempted.

9/AB/9 (Item 3 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

04322433 Genuine Article#: RV296 Number of References: 28
Title: UPTAKE AND DISTRIBUTION OF N-ACETYLCYSTEINE IN MICE - TISSUE-SPECIFIC EFFECTS ON GLUTATHIONE CONCENTRATIONS (Abstract Available)
Author(s): MCLELLAN LI; LEWIS AD; HALL DJ; ANSELL JD; WOLF CR
Corporate Source: UNIV DUNDEE,NINEWELLS HOSP & MED SCH,BIOMED RESCTR/DUNDEE DD1 9SY//SCOTLAND/; UNIV GLASGOW,CRC DEPT MED ONCOL/GLASGOW G61

1BD/LANARK/SCOTLAND/; HERIOT WATT UNIV,SYNTEX RES CTR/EDINBURGH EH14 4AP/MIDLOTHIAN/SCOTLAND/; UNIV EDINBURGH,INST CELL ANIM & POPULAT BIOL,ASHWORTH LABS/EDINBURGH EH9 3JT/MIDLOTHIAN/SCOTLAND/; UNIV DUNDEE,NINEWELLS HOSP & MED SCH,BIOMED RESCTR,IMPERIAL CANC RES FUND MOLEC PHARMACOL UNIT/DUNDEE DD1 9SY//SCOTLAND/
Journal: CARCINOGENESIS, 1995, V16, N9 (SEP), P2099-2106
ISSN: 0143-3334
Language: ENGLISH Document Type: ARTICLE
Abstract: Modulation of cellular thiols has been used to ameliorate the toxic side effects associated with cancer chemotherapy and is currently being investigated as a novel therapeutic strategy in cancer treatment. One of the most extensively studied modulators of thiol levels is N-acetylcysteine (NAC), a cytoprotective drug with multiple therapeutic applications, including use as an adjunct to cancer chemotherapy. Tissue-specific protective effects have previously been observed when NAC has been used in conjunction with chemotherapeutic alkylating agents, but the basis for this was unknown. In view of the contrasting cytoprotective effects of NAC in bladder and bone marrow we examined the effect of this compound on mouse liver, bladder and bone marrow glutathione (GSH) levels, as well as the disposition of C-14-labelled NAC. Radiolabelled NAC was taken up by the majority of tissues at varying rates and levels, except for the brain and spinal cord. The bladder, bone marrow and liver all took up the drug or its metabolites within 15 min of injection, NAC was not found to alter GSH concentrations in the liver, but increased GSH levels in the bladder similar to 2-fold. In contrast, the GSH content of bone marrow was found to decrease by 70-50% after NAC administration. When separate bone marrow cell populations were examined the decrease in GSH was associated with granulocytes, as opposed to lymphocytes, whose GSH levels remained unchanged. These findings provide a possible explanation for the differential cytoprotective effects of NAC.

9/AB/10 (Item 4 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

04295701 Genuine Article#: RV099 Number of References: 40
Title: TRANSDUCTION OF NIH 3T3 CELLS WITH A RETROVIRUS CARRYING BOTH HUMAN MDR1 AND GLUTATHIONE -S- TRANSFERASE -PI PRODUCES BROAD-RANGE MULTIDRUG-RESISTANCE (Abstract Available)
Author(s): DOROSHOW JH; METZ MZ; MATSUMOTO L; WINTERS KA; SAKAI M; MURAMATSU M; KANE SE
Corporate Source: CITY HOPE NATL MED CTR,DEPT CELL & TUMOR BIOL,1500 E DUARTE RD/DUARTE//CA/91010; CITY HOPE NATL MED CTR,DEPT CELL & TUMOR BIOL/DUARTE//CA/91010; CITY HOPE NATL MED CTR,DEPT MED ONCOL & THERAPEUT RES/DUARTE//CA/91010; HOKKAIDO UNIV,SCH MED,DEPT BIOCHEM/SAPPORO/HOKKAIDO 060/JAPAN/; SAITAMA MED SCH,DEPT BIOCHEM/MOROYAMA/SAITAMA 35004/JAPAN/
Journal: CANCER RESEARCH, 1995, V55, N18 (SEP 15), P4073-4078
ISSN: 0008-5472
Language: ENGLISH Document Type: ARTICLE
Abstract: In these experiments, we examined the ability of a retroviral vector, pHaMASV, to encode two potential chemoprotective genes on separate transcription units. We previously described the pHaMSV vector, which includes the human MDR1 gene as a selectable marker and chemoprotective gene, plus an internal SV40 promoter for expressing a second heterologous gene along with MDR1 [M. E. Metz, D. M. Best, and S. E. Kane. Virology, 208: 634-643, 1995]. To test the ability of this vector to deliver two therapeutic genes simultaneously, the cDNA for human glutathione S- transferase pi (GST pi, the most abundant

member of the glutathione S- transferase family in human tumor cells) was inserted into pHaMASV, and this plasmid was transfected into ecotropic packaging cells. The resulting pHaMASV.GST pi ecotropic retrovirus, which was produced at a titer of 2 x 10(6) colony-forming units/ml, was used to transduce NIH 3T3 cells. After initial selection in 60 ng/ml colchicine, a population of transduced cells was exposed to stepwise increasing colchicine concentrations to select for amplified expression of MDR1. As MDR1 expression increased, the expression of GST increased in concert, as demonstrated by Northern analysis, Western analysis, and measurements of glutathione S- transferase activity, Transduced cells growing in 1280 ng/ml colchicine had about 3-fold higher total glutathione S- transferase activity than nontransduced cells and 2.5-fold higher activity than transduced cells growing in 60 ng/ml colchicine. Northern hybridizations demonstrated a 3-5-fold increase in both the full-length retroviral message encoding MDR1 and the subgenomic mRNA encoding GST pi. after amplification of resistance from 60 to 1280 ng/ml colchicine. The cytotoxic effects of several xenobiotics were evaluated in NIH 3T3 cells transfected with MDR1 (3T3.MDR) or transduced with the MDR1-GST pi retrovirus (3T3.GST640 or 3T3.GST1280) to evaluate the ability of our vector to produce a spectrum of drug resistances specific for the genes expressed, 3T3.MDR and 3T3.GST1280 cells expressing equivalent levels of MDR1 had identical levels of resistance to doxorubicin or colchicine. These results suggest that GST pi; expression did not contribute to doxorubicin resistance in this model system. However, 3T3.GST640 cells were about 4-fold resistant to ethacrynic acid and 1-chloro-2,4-dinitrobenzene compared to cells expressing MDR1 alone, consistent with the ability of GST pi to conjugate both of these cytotoxins. Increases in drug resistance paralleled increases in gene-specific mRNA and recombinant protein levels in all cases. Thus, our studies suggest that the amplifiable coexpression of MDR1 plus a second potentially therapeutic gene of interest is a feasible strategy for the delivery of multiple drug resistance genes to normal cells for protection against the toxic side effects of combination chemotherapy .

9/AB/11 (Item 5 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

01307945 Genuine Article#: GM859 Number of References: 32
Title: DRUG RESISTANCE-REVERSAL STRATEGIES - COMPARISON OF EXPERIMENTAL-DATA WITH MODEL PREDICTIONS (Abstract Available)
Author(s): SLATE D; MICHELSON S
Corporate Source: SYNTEX INC,INST RES DATA MANAGEMENT/PALO ALTO//CA/94303; SYNTEX INC,INST RES DATA MANAGEMENT/PALO ALTO//CA/94303; SYNTEX INC,INST CANC & DEV BIOL/PALO ALTO//CA/94303
Journal: JOURNAL OF THE NATIONAL CANCER INSTITUTE, 1991, V83, N21, P 1574-1580
Language: ENGLISH Document Type: ARTICLE
Abstract: We previously developed a mathematical model to describe the emergence and dynamic growth of a drug-resistant subpopulation in a tumor. In the present study, our objective was to test the model's ability to mimic two strategies for reversal of drug resistance. We present data from one in vitro cell proliferation assay with drug-resistant LS174T human colon carcinoma variants and one in vivo assay of survival after treatment of female (C57BL/6 x DBA/2)F1 mice inoculated with doxorubicin-resistant P388/ADR leukemia cells. The in vitro assay examined the effects of inhibiting the biosynthesis of glutathione in cells resistant to alkylating agents or cisplatin. The

in vivo assay compared the effects on cell survival of low-level continuous infusion versus high-intensity bolus dosing, with or without coadministration of the drug efflux pump blocker verapamil. Results in vitro and in vivo were comparable for qualitative accuracy and predictability to results with the model. Both the in vitro study and the model showed that, for resistant cells with high levels of glutathione, short-term cell survival was dose dependent and that even high doses of drug did not eliminate all of these cells. Addition of an inhibitor of glutathione biosynthesis did, however, augment elimination of the resistant cells. Resistant cells with low levels of glutathione could be eliminated with high drug doses or coadministration of drug and a glutathione synthesis inhibitor. In vivo, coadministration of doxorubicin with verapamil increased animal survival when either continuous infusion or bolus dosing regimens were used. The effectiveness of the blocker is crucial; when a partially (50%) effective blocker is used, continuous infusion achieves better elimination of resistant cells, but a completely (100%) effective blocker is efficacious in both dosing scenarios. Careful interpretation of these findings is necessary because the pharmacokinetics of drug in the small populations of cells in the model are not easily extrapolated to those in large tumors. This model may be useful in determining resistance mechanisms, their levels of effectiveness, and concentrations of compounds required at target sites to overcome them.

9/AB/12 (Item 6 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

00523556 Genuine Article#: DZ058 Number of References: 38
Title: ANALYSIS OF CLASS-II (HYDROLYTIC) AND CLASS-I (BETA-LYASE) APURINIC APYRIMIDINIC ENDONUCLEASES WITH A SYNTHETIC DNA SUBSTRATE
Author(s): LEVIN JD; DEMPLE B
Corporate Source: HARVARD UNIV,DEPT BIOCHEM & MOLEC BIOL/CAMBRIDGE//MA/02138; HARVARD UNIV,DEPT BIOCHEM & MOLEC BIOL/CAMBRIDGE//MA/02138
Journal: NUCLEIC ACIDS RESEARCH, 1990, V18, N17, P5069-5075
Language: ENGLISH Document Type: ARTICLE

9/AB/13 (Item 1 from file: 71)
DIALOG(R)File 71:ELSEVIER BIOBASE

00751083 97258765
Fibronectin fragment-facilitated retroviral transfer of the Glutathione -S- Transferase Pi gene into CD34sup + cells to protect them against alkylating agents
Kuga T.; Sakamaki S.; Matsunaga T.; Hirayama Y.; Kuroda H.; Takahashi Y.; Kusakabe T.; Kato I.; Niitsu Y.
ADDRESS: Dr. Y. Niitsu, 4th Department of Internal Medicine, Sapporo Medical Univ. Sch. Medicine, South-1, West-16, Chuou-ku, Sapporo 060, Japan
Journal: Human Gene Therapy, 8/16 (1901-1910), 1997, United States
PUBLICATION DATE: 19970000
CODEN: HGTHE
ISSN: 1043-0342
DOCUMENT TYPE: Article
LANGUAGES: English SUMMARY LANGUAGES: English
NO. OF REFERENCES: 40

To protect bone marrow cells from the toxicity of chemotherapy , a multidrug resistant gene or a dihydrofolate reductase gene has been introduced into stem cells. These genes, however, are not capable of conferring refractoriness to alkylating agents (AA), which are some of the most commonly used agents in chemotherapy regimens. In the present study, an attempt was made to endow human stem cell (CD34sup + cells) with resistance to cyclophosphamide, a well-known AA, and adriamycin (ADM) by transducing the glutathione -S- transferase Pi (GST-Pi) gene whose product is thought to detoxify AA by conjugating them with glutathione and to remove a toxic peroxide formed by ADM. The gene transduction was carried out retrovirally with a virus titer of 1 x 10sup 5 FFU/ml, employing a recombinant fibronectin fragment; transduction efficiency was extremely low without the fragment. Incubation with interleukin-6 and stem cell factor enhanced the expression of fibronectin ligands VLA4 and VLA5 on CD34sup + cells. This enhanced expression of VLA4 and VLA5 was considered to facilitate a close contact of the CD34sup + cell to the retroviral vector via fibronectin fragments and the subsequent transduction process. The GST-Pi gene-transduced CD34sup + cells formed almost 3- and 2.5-fold more CFU-GM than neo gene-transduced CD34sup + cells in the presence of 2.5 mug/ml of 4-hydroperoxycyclophosphamide (4-HC), an active form of cyclophosphamide, and 30 ng/ml ADM, respectively. The transfectants formed an appreciable number of colonies, even at higher concentrations of these drugs (5.0 mug/ml of 4-HC, 50 ng/ml of ADM) whereas neo gene-transduced or nontransduced CD34sup + cells formed no colonies at all, indicating the possibility of selecting out the transfectants by exposing them to these anticancer drugs. Thus, we were able to demonstrate that transduction of the GST-Pi gene confers resistance to cyclophosphamide as well as to ADM, and therefore this approach can be applied clinically for high-dose chemotherapy.

9/AB/14 (Item 1 from file: 73)
DIALOG(R)File 73:EMBASE

05905143 EMBASE No: 1994323599
P glycoprotein-mediated multidrug resistance in normal and neoplastic hematopoietic cells
Licht T.; Pastan I.; Gottesman M.; Herrmann F.
Dept Med Oncol Applied Molec Biology, Universitatsklinikum Rudolf Virchow, Robert-Rossle-Cancer-Center, Lindenberger Weg 80,D-13122 Berlin Germany
Annals of Hematology (ANN. HEMATOL.) (Germany) 1994, 69/4 (159-171)
CODEN: ANHEE ISSN: 0939-5555
DOCUMENT TYPE: Journal; Review
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

The multidrug transporter, P-glycoprotein (P-gp), is expressed by CD34 -positive bone marrow cells, which include hematopoietic stem cells, and in other cells in the bone marrow and peripheral blood including some lymphoid cells. Multidrug resistance mediated by P-gp appears to be a major impediment to successful treatment of acute myeloid leukemias and multiple myelomas. However, the impact of P-gp expression on prognosis has to be confirmed in several other hematopoietic neoplasms. The role of P-gp in normal and malignant hematopoiesis and clinical attempts to circumvent multidrug resistance in hematopoietic malignancies are reviewed. The recent transduction of the MDR1 gene into murine hematopoietic cells, which protects them from toxic effects of chemotherapy , suggests that MDR1 gene therapy may help prevent myelosuppression following chemotherapy.

9/AB/15 (Item 1 from file: 76)
DIALOG(R)File 76:Life Sciences Collection

02220822 4248641
Fibronectin fragment-facilitated retroviral transfer of the glutathione -S- transferase pi gene into CD34 super(+) cells to protect them against alkylating agents
Kuga, T.; Sakamaki, S.; Matsunaga, T.; Hirayama, Y.; Kuroda, H.; Takahashi, Y.; Kusakabe, T.; Kato, I.; Niitsu, Y.
4th Dep. Intern. Med., Sapporo Med. Univ. Sch. Med., South-1, West-16, Chuo-ku, Sapporo, 060, Japan
HUM. GENE THER. vol. 8, no. 16, pp. 1901-1910 (1997)
ISSN: 1043-0342
DOCUMENT TYPE: Journal article LANGUAGE: ENGLISH
SUBFILE: Medical and Pharmaceutical Biotechnology Abstracts; Genetics Abstracts

To protect bone marrow cells from the toxicity of chemotherapy , a multidrug resistant gene or a dihydrofolate reductase gene has been introduced into stem cells. These genes, however, are not capable of conferring refractoriness to alkylating agents (AA), which are some of the most commonly used agents in chemotherapy regimens. In the present study, an attempt was made to endow human stem cell (CD34 super(+) cells) with resistance to cyclophosphamide, a well-known AA, and adriamycin (ADM) by transducing the glutathione -S- transferase pi (GST- pi) gene whose product is thought to detoxify AA by conjugating them with glutathione and to remove a toxic peroxide formed by ADM. The gene transduction was carried out retrovirally with a virus titer of 1 x 10 super(5) FFU/ml, employing a recombinant fibronectin fragment transduction efficiency was extremely low without the fragment. Incubation with interleukin-6 and stem cell factor enhanced the expression of fibronectin ligands VLA4 and VLA5 on CD34 super(+) cells. This enhanced expression of VLA4 and VLA5 was considered to facilitate a close contact of the CD34 super(+) cell to the retroviral vector via fibronectin fragments and the subsequent transduction process. The GST- pi gene-transduced CD34 super(+) cells formed almost 3- and 2.5-fold more CFU-GM than neo gene-transduced CD34 super(+) cells in the presence of 2.5 mu g/ml of 4-hydroperoxycyclophosphamide (4-HC), an active form of cyclophosphamide, and 30 ng/ml ADM, respectively. The transfectants formed an appreciable number of colonies, even at higher concentrations of these drugs (5.0 mu g/ml of 4-HC, 50 ng/ml of ADM) whereas neo gene-transduced or nontransduced CD34 super(+) cells formed no colonies at all, indicating the possibility of selecting out the transfectants by exposing them to these anticancer drugs. Thus, we were able to demonstrate that transduction of the GST- pi gene confers resistance to cyclophosphamide as well as to ADM, and therefore this approach can be applied clinically for high-dose chemotherapy.

9/AB/16 (Item 1 from file: 144)
DIALOG(R)File 144:Pascal

15104745 PASCAL No.: 01-0265130
The pharmacological phenotype of combined multidrug-resistance mdr1a/1b- and mrp1-deficient mice
JOHNSON Dennis R; FINCH Rick A; PING LIN Z; ZEISS Caroline J; SARTORELLI Alan C
Department of Pharmacology and Developmental Therapeutics Program, Cancer Center and Section of Comparative Medicine, Yale University School of Medicine, New Haven, Connecticut 06520, United States

Journal: Cancer research : (Baltimore), 2001, 61 (4) 1469-1476
Language: English

Two major classes of plasma membrane proteins that actively extrude a wide range of structurally diverse hydrophobic amphipathic antineoplastic agents from cells, with different mechanisms of action, lead to multidrug resistance. To study the importance of these ATP-binding cassette transporters to the toxicity of cancer chemotherapy agents, we have used mice genetically deficient in both the mdr1a and mdr1b genes (mdr1a/1b(-/-) mice), the mrp1 gene (mrp1(-/-) mice), and the combined genes mdr1a/1b and mrp1 (mdr1a/1b(-/-), mrp1(-/-) mice) and embryonic fibroblasts derived from wild-type mice and from the three gene knockout animals. The consequences of export pump deficiencies were evaluated primarily using vincristine and etoposide. Mice deficient in the three genes, mdr1a/1b and mrp1, exhibited a 128-fold increase in toxicity to vincristine and a 3-5-fold increase in toxicity to etoposide; increased toxicity to embryonic fibroblast cells from triple knockout mice also occurred with vincristine and etoposide. Vincristine, which normally does not express toxicity to the bone marrow and to the gastrointestinal mucosa when used at therapeutic doses, caused extensive damage to these tissues in mdr1a/1b(-/-), mrp1(-/-) mice. The findings indicate that the P-glycoprotein and mrp1 are compensatory transporters for vincristine and etoposide in the bone marrow and the gastrointestinal mucosa and emphasize the potential for increased toxicities by the combined inhibition of these efflux pumps.

9/AB/17 (Item 1 from file: 149)
DIALOG(R)File 149:TGG Health&Wellness DB(SM)

01991323 SUPPLIER NUMBER: 74521084 (USE FORMAT 7 OR 9 FOR FULL TEXT)
Working towards tailored therapy for cancer.(News)(Brief Article)
Hutchinson, Ezzie
The Lancet, 357, 9267, 1508
May 12,
2001
DOCUMENT TYPE: Brief Article PUBLICATION FORMAT: Magazine/Journal; Refereed ISSN: 0099-5355 LANGUAGE: English RECORD TYPE: Fulltext
TARGET AUDIENCE: Professional
WORD COUNT: 993 LINE COUNT: 00087

9/AB/18 (Item 2 from file: 149)
DIALOG(R)File 149:TGG Health&Wellness DB(SM)

01879811 SUPPLIER NUMBER: 58614457 (USE FORMAT 7 OR 9 FOR FULL TEXT)
Pharmacogenomics.
Sadee, Wolfgang
The Western Journal of Medicine, 328
Nov,
1999
PUBLICATION FORMAT: Magazine/Journal; Refereed ISSN: 0093-0415
LANGUAGE: English RECORD TYPE: Fulltext TARGET AUDIENCE: Professional
WORD COUNT: 3158 LINE COUNT: 00317

9/AB/19 (Item 3 from file: 149)
DIALOG(R)File 149:TGG Health&Wellness DB(SM)

01863889 SUPPLIER NUMBER: 56744314 (USE FORMAT 7 OR 9 FOR FULL TEXT)
Primary Central Nervous System Tumors: Advances in Knowledge and Treatment.
Prados, Michael D.; Berger, Mitchell S.; Wilson, Charles B.
Ca, 48, 6, 331
Nov,
1998
PUBLICATION FORMAT: Magazine/Journal; Refereed ISSN: 0007-9235
LANGUAGE: English RECORD TYPE: Fulltext TARGET AUDIENCE: Academic; Professional
WORD COUNT: 12821 LINE COUNT: 01121

9/AB/20 (Item 4 from file: 149)
DIALOG(R)File 149:TGG Health&Wellness DB(SM)

01803499 SUPPLIER NUMBER: 20755160 (USE FORMAT 7 OR 9 FOR FULL TEXT)
Conventional cancer therapy: promise broken or promise delayed?(The Promise of Cancer Research and Treatment)
Tannock, Ian F.
The Lancet, v351, n9114, pS9(8)
May 16,
1998
PUBLICATION FORMAT: Magazine/Journal; Refereed ISSN: 0099-5355
LANGUAGE: English RECORD TYPE: Fulltext; Abstract TARGET AUDIENCE: Professional
WORD COUNT: 7049 LINE COUNT: 00598

ABSTRACT: Surgery, chemotherapy, and radiation remain the mainstay of cancer treatment, despite the growing interest in biological and gene therapies. Improved surgical techniques and focused radiation therapy have reduced the damage to healthy tissue and preserved normal organ function, as in lumpectomy for breast cancer. Research on the molecular response of tumor cells to radiation may improve the effectiveness of radiotherapy. Research on the cellular response to chemotherapy drugs, and better testing models, can lead to better-targeted and more effective treatment regimens.

9/AB/21 (Item 5 from file: 149)
DIALOG(R)File 149:TGG Health&Wellness DB(SM)

01740395 SUPPLIER NUMBER: 20132709 (USE FORMAT 7 OR 9 FOR FULL TEXT)
Glutathione -S- transferase pi gene transfer protects CD34 + cells. (drug resistance against alkylating agents)
Marble, Michelle
Cancer Weekly Plus, p15(2)
Dec 15,
1997
PUBLICATION FORMAT: Newsletter LANGUAGE: English RECORD TYPE: Fulltext
TARGET AUDIENCE: Professional
WORD COUNT: 626 LINE COUNT: 00056

9/AB/22 (Item 6 from file: 149)
DIALOG(R)File 149:TGG Health&Wellness DB(SM)

01606185 SUPPLIER NUMBER: 17632038 (USE FORMAT 7 OR 9 FOR FULL TEXT)

Therapeutic transfection of two genes possible.
Marble, Michelle
Cancer Biotechnology Weekly, p3(2)
Nov 6,
1995
PUBLICATION FORMAT: Magazine/Journal LANGUAGE: English RECORD TYPE: Fulltext TARGET AUDIENCE: Professional
WORD COUNT: 639 LINE COUNT: 00057

9/AB/23 (Item 7 from file: 149)
DIALOG(R)File 149:TGG Health&Wellness DB(SM)

01300354 SUPPLIER NUMBER: 11014845 (USE FORMAT 7 OR 9 FOR FULL TEXT)
Drug resistance. (Research Report)
Cowan, Kenneth
Cancer Weekly, p20(1)
July 15,
1991
PUBLICATION FORMAT: Newsletter LANGUAGE: English RECORD TYPE: Fulltext
TARGET AUDIENCE: Professional
WORD COUNT: 396 LINE COUNT: 00040

9/AB/24 (Item 1 from file: 351)
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Modulating haematopoiesis - by admin. of glutathione deriv. to bone marrow or peripheral blood, to protect against destructive effects of chemo- or radio-therapy
Patent Assignee: TELIK INC (TELI-N); TERRAPIN TECHNOLOGIES INC (TERR-N)
Inventor: BORCH R F; KAUVAR L M; LYTTLE M H; MORGAN A S
Number of Countries: 066 Number of Patents: 006
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week	
WO 9640205	A1	19961219	WO 96US9057	A	19960605	199705	B
ZA 9604755	A	19970226	ZA 964755	A	19960606	199714	
AU 9660481	A	19961230	AU 9660481	A	19960605	199716	
US 5767086	A	19980616	US 92863564	A	19920403	199831	
			US 93126229	A	19930924		
			US 94305993	A	19940919		
			WO 94US10797	A	19940923		
			US 95482645	A	19950607		
JP 11507056	W	19990622	WO 96US9057	A	19960605	199935	
			JP 97501468	A	19960605		
AU 715524	B	20000203	AU 9660481	A	19960605	200016	

Priority Applications (No Type Date): US 96636516 A 19960419; US 95482645 A 19950607; US 92863564 A 19920403; US 93126229 A 19930924; US 94305993 A 19940919; WO 94US10797 A 19940923
Patent Details:

Patent No	Kind	Lan	Pg	Main IPC	Filing Notes
WO 9640205	A1	E	72	A61K-038/06	
Designated States (National): AL AM AU BB BG BR CA CN CZ EE GE HU IL IS JP KG KP KR LK LR LT LV MD MG MK MN MX NO NZ PL RO SG SI SK TR TT UA UZ VN					
Designated States (Regional): AT BE CH DE DK EA ES FI FR GB GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG					
AU 715524	B			A61K-038/06	Previous Publ. patent AU 9660481 Based on patent WO 9640205
ZA 9604755	A		71	A61K-000/00	
AU 9660481	A				Based on patent WO 9640205
US 5767086	A			A61K-038/06	CIP of application US 92863564 CIP of application US 93126229 CIP of application US 94305993 CIP of application WO 94US10797 CIP of patent US 5599903
JP 11507056	W		61	A61K-038/00	Based on patent WO 9640205

Abstract (Basic): WO 9640205 A

Modulating haematopoiesis in bone marrow , peripheral blood or fractions, protecting against the destructive effects of chemotherapeutic agent (CA) or irradiation (IR) or potentiating effects of CA comprises admin. of glutathione deriv. of formula (I) or the ester, amide, ester/amide or salt form.

YCO = gamma -Glu or beta -Asp,

G' = phenylglycine or Gly,

Z = CH2, O or S and

X = 1-20C hydrocarbon.

Also claimed are:

(1) a method of modulating haematopoiesis or protecting effects of CAs, contacting bone marrow or peripheral blood or haematopoietic progenitor cell-contg. fraction with a cpd. which inhibits at least 1 glutathione S- transferase , isoenzyme subclass, and

(2) a unit dosage form compsn. contg. (I) or its ester, amide, ester/amide or salt.

USE - (I) are glutathione S- transferase inhibitors used to modulate haematopoiesis in bone marrow , mitigate the bone marrow destructive effects of a chemotherapeutic agent and potentiate toxicity of chemotherapeutic agents. They are used as aids to chemotherapeutic treatment of tumours by protecting the haematopoietic system w.r.t. toxic agents which are used in chemotherapy . The cpds. are orally active. Patients benefitting from (I) include those whose bone marrow progenitor cells are inadequate in number or physiological status to sustain differentiation in partic. where the subject has been exposed to bone marrow destructive agents such as chemotherapeutic agents, radiation, exposure to toxins in the environment and in patients with bone marrow degenerative diseases and conditions e.g. in patients undergoing chemotherapy, immuno-compromised patients, patients showing symptoms of anaemia, neutropenia, thrombocytopenia or lack of adequate platelet levels and prospective subjects for treatment with cytotoxic agents. Dosage is 0.1-100 (esp. 1-10) mg/kg. for 10-40 (esp. 14-28) days. Admin. is carried out i.p., i.v. or oral. The oral compsn. is in the form of a tablet, pill, capsule, syrup, powder or tonic (all claimed).

Dwg.10/17

9/AB/25 (Item 1 from file: 434)
DIALOG(R)File 434:SciSearch(R) Cited Ref Sci

08735600 Genuine Article#: N0073 Number of References: 270
Title: CHEMICAL MODIFIERS OF CANCER-TREATMENT
Author(s): COLEMAN CN; BUMP EA; KRAMER RA
Corporate Source: HARVARD UNIV,SCH MED,JOINT CTR RADIAT THERAPY,50 BINNEY ST/BOSTON//MA/02115
Journal: JOURNAL OF CLINICAL ONCOLOGY, 1988, V6, N4, P709-733
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